

Part of 28/A

VS GGSINSGDYNNWIRQHPEKGLDCIGYIYSGSTYNNPSLKSRTVISVDTSKNQF F LKL TSVTAADTAVYYCARSTVNPNGWFDPMGGGTLVTYSS (SEQ ID NO: 23)

CDR1

CDR2

CDR3

FIG. 1

GTCTCTGGTG GCTCCATCAA CAGTGGTGAT TACTACTGGA GCTGGATCCG CCAGCACCCA GGGAGGGCC TGGACTGCAT TGGGTACATC TATTACAGTG GGAGCACCTA CTACACCCG
TCCCTCAAGA GTGAGTTAC CATATCAGTA GACAGTCTA AGATCAGTT CTTCCTGAAG CTGACTCTG TGA CTGCTG GACACGGCC GTGTATTACT GTGGAGATC TACGGTGTA
AATCCGGGGT GGTTCGACCC CTGGGGCCAR GGAACCTGG TCACCGTCTC CTCA (SEQ ID NO: 3)

FIG. 2

TTTCQASDDINNYLNWFQKPGKAPK VLIHDSNLETGGPSRFSGSGTDFTTISGLQPEDIATYYCQY E S L P L T F G G G T K V E I K R T V A P S V F I P P S D E Q (SEQ ID NO: 24)

CDR1

CDR2

CDR3

FIG. 3

ACCATCACTT GCCAGGCGAG TCAGGACATT AACAACTATT TAAATTGGTT TCAGCAGAAA CCAGGGAAG CCCT AAGGTCCTGA TCCACGATGC ATCCAATTG GAAACAGGG
GCCCATCAAG GTTCAGTGA AGTGGATCTG GGACA GATTTACTT TCACCATCAG CGGCTGCAG CCTGAAGACA TTGCACATA TTATTGTCAA CAGTATGAAA GTCTC CCACCTCACTT
TCGGCGGAGG GACCAAGGTG GAGATCAAA (SEQ ID NO: 4)

FIG. 4

VSGGSINSGDYVWSVIRQHPGKLEWIGSIYSGNIFYNPSLKSRVTISLDTSKNQFSLKSSVTAADTAVCYCARNIVTTGAEDINGGGTMVTYSS (SEQ ID NO: 25)

CDR1 CDR2 CDR3

FIG. 5

GTCTCTGGTG GCTCCATCAA CAGTGGTGAT TACTACTGGA GCTGGATCCG CCAGCACCCA GGGAGGGGCC TGGAGTGGAT TGGGTCCATC TATTACAGTG GGAACACCTT CTACAACCCG
TCCCTCAAGA GTCCAGTTAC CATATCACTA GACACGTCTA AGAACCAATT CTCCTGAAG CTGAGTTCTG TGA CTGCGC GGAACACGGCC GTGTGTTACT GTGGAGAGAA TATAGTACT
ACGGGTGCTT TTGATATCTG GGGCCAAGGG ACAATGGTCA CCGTCTCTTC A (SEQ ID NO: 5)

FIG. 6

TTTCQASQDIT IYLNWYQKPKAPKLLINDASSLETGVP LRFSGSGSDTFTFTISSLPEDIAITYYQQYDHLPLTFGGGTKVAIKRTVAAPSVFIFPPSDEQ (SEQ ID NO: 26)

CDR1 CDR2 CDR3

FIG. 7

ACCATCATT GTCAGGGGAG TCAGGACATT ACCATTATT TAAATTGTA TCAACAGAAA CCAGGGAAG CCCCT AGGTCCTGA TCAACGACGC ATCCAGTTTG GAAACAGGGG
TCCATTAAAG GTTCAGTGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAG CAGCCTGCAG CCTGAAGATA TTGCAACATA TTACTGTCAA CAGTATGATC ATCTC CCGCTCATT
TCGGCGGGCGG GACCAAGGTG GCGATCAAA (SEQ ID NO: 6)

FIG. 8

VSGGSISSG DYYW T V I R Q H P G K G L E N I G Y I Y Y S G N T Y Y N P S L K S R V S M S I D T S E N Q F S L K L S S V T A A D T A V Y Y C A R K P V T G G E D Y V G G G T L V T V S S (SEQ ID NO: 27)

CDR1

CDR2

CDR3

FIG. 9

G T C T C T G G T G G T C C A T C A G C A G T G G T G A T T A C T A C T G G A C C A C C C A G G A A G G G C C T G G A T C C G C C A G C A C C C A T T A T T A C A G T G G A C A C C C T A C T A C A C C C G
 T C C C T C A A G A G T C G A G T T C C A T G C A A T A G A C A G T T C T C C T G A A G C T G A G C T C T G T G A C T G C C G G G A C A G G C C G T G T A T T A C T G T G G A G A A A A C C A G T G A C T
 G G G G G G A G G A C T A C T G G G G C C A G G G A A C C C T G G T C A C C G T C T C C T C A (SEQ ID NO: 7)

FIG. 10

T I T C Q A S O D I S N Y L N W Y Q K P G K A P K L L I Y D A S N L E T G V P S R F S G S G T D F T F T I S S L Q P E D I V G Y Y V Q R Y E S L P C G F G G G T K L E I K R T V A P S V F I F P P S D E Q (SEQ ID NO: 28)

CDR1

CDR2

CDR3

FIG. 11

A C C A T C A C T T G C A G G C G A G T C A G G A C A T T A G T A A C T A T T T A A T T G G T A T C A G C A G A A A C C A G G A A G C C C T A N G C T C C T G A T C I A C G A T G C T T C C A A T T T G G A A C A G G G G T C C C A T C A A G
 G T T C A G T G G A G T G G A T C T G G A C A T T C A C C A T C A G C A G C C T G C A G C C T G A A G A T G T G G A A C A T A T G T C T G T C A A C A G T A T G A G A G T C C C G T G C G G T T T T G G C C A G G G
 G A C C A A A C T G G A G A T C A A A (SEQ ID NO: 8)

FIG. 12

VSGGSI^{NSG}DF^{YWSVIRQHPCKGLEWIGYIYSGSYNPSLKSRYVT}^{Ms}^{IdP}^{SKNQFSLKL}^{ISVTAADTAVYYCA}^T^{SLYYGGGMDVWGQGT}^{TVTVSS} (SEQ ID NO: 29)

CDR1

CDR2

CDR3

FIG. 13

GTCTCTGGTG GCTCCATCAA CAGTGGTGAT TTCTACTGGA GCTGGATCCG CCAACACCCA GGAAGGGCC TGGAGTGGAT TGGGTACATC TATTACAGTG GGAGCACCTA CTACAACCCG
TCCCTCAAGA GTCGAGTTAC CATGTCAATA GACCCGTCTA AGACCAAGTT CTCCTGAAA CTGATCTCTG TGA CTGCCG GACACGGCC GTTTATTACT GTGGACNTC CCTTTACTAT
GGCGGGGGTA TGGACGCTCTG GGGCCAAGG ACCACGGTCA CCGTCTCCTC A (SEQ ID NO: 9)

FIG. 14

TTTCAASDDIS^{NL}NWYQQR^{Rg}NAPKLLIYDASNIETGVPSPFSGSGSDTFTFTIS^{NL}QPEDIAITYYCA^HYD^HLPWTFGGGTVKXKRTVAAPSVFI^{PPS}DEQ (SEQ ID NO: 30)

CDR1

CDR2

CDR3

FIG. 15

ACCATCACTT GCCAGGCGAG TCAGGACATT AACACTATT TGAATTGGTA TCAGCAGAGG CNGGGAGCG CCGCT AAACCTCCIGA TCTACGATGC ATCCAATTG GAAACAGGGG
TCCCATCAAG GTTCAGTGGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAA CAGCCTGCAG CCTGAAGATA TTGGACATA TTATTGTCAA CACTATGATC ATCTC CCGTGGACGT
TCGGCCAAGG GACCAAGGTG GAANTCAAA (SEQ ID NO: 10)

FIG. 16

VSGGSINNGDYYSVIRQHPGKLEWIGHIYYSGSTYYIPSLKSR T TISVDTSKNQFSLKLN SVTAADIAVYYCARGTVITTYFYDYWGQGTTVTVSS (SEQ ID NO: 31)
CDR1 CDR2 CDR3

FIG. 17

GTCTCTGGTG GCTCCATCAA CAATGGTGAT TACTACTGGA GCTGGATCCG CCAGCACCCA GGAAGGGCC TGGAGTGGAT TGGGCACATC TATTACAGTG GGAGCACCTA CTACATCCCC
TCCCTCAAGA GTCGAACTAC CATATCAGTA GACAGTCTA AGAACCAATT CTCCTGAAG CTGAACCTGT TGACTGCCGC GGACACGGCC GTGTATTACT GTGCGAGAGG GACAGTAACT
ACGTACTACT TTGACTACTG GGGCCAGGGA ACCCTGGTCA CCGTCTCCTC A (SEQ ID NO: 11)

FIG. 18

TTTCRASQSISSYLNWYQKPKAPKLLIYAASSLQSGVPSRFSGSGGTDFTLTISLQPEDFATYYCQQ GyRTPPECSFGGTKLEIKRTVAAPSV IFPPSDEQ (SEQ ID NO: 32)
CDR1 CDR2 CDR3

FIG. 19

ACCATCACTT GCCGGGCAAG TCAGAGCATT AGCAGCTATT TAAATTGGTA TCAGCAGAAA CCAGGGAAG CCCCT AAGCTCCTGA TCTATGCTGC ATCCAGTTTG CAAAGTGGGG
TCCCATCAAG GTTCAGTGGC AGTGGATCTG GGACA GATTTCATC TCACCATCAG CAGTCTGCAA CCTGAAGATT TTGCAACTTA CTACTGTCAA CAGGGTTACA GAACC CCTCCGGAGT
GCAGTTTTTG CCAGGGGACC AAGCTGGAGA TCAAA (SEQ ID NO: 12)

FIG. 20

VSGGSVSSG DYYWSWIRQPPGKGLWIGHL YYSGNTNYPNPSLKSRVTISL DTSKNQFSLKLSVTAADTAVYYCARDFL IGSFFDYWGGLTVTVSS (SEQ ID NO: 33)
CDR1 CDR2 CDR3

FIG. 21

GTCTCTGGTG GCTCCGTCAG CAGTGGTGAT TACTACTGGA GCTGGATCCG GCAECCCCCA GGAAGGGAC TGGAGTGGAT TGGACATCTC TATTACAGTG GGAACACCAA CTACAACCCC
TCCCTCAAGA GTCGAGTCAC CATATCATT GACAGTCCA AGAACAGT CTCCTGAAG CTGAGCTCTG TGACCGCTGC GGACACGGCC GTGTATTACT GTGCGAGAGA TTTTGTGACT
GGTTCCCTTCT TTGACTACTG GGGCCAGGGA ACCCTGGTCA CCGTCTCCTC A (SEQ ID NO: 13)

FIG. 22

TTTCAASQDI SNYLNWYQKPKGKAPKLLIN NDASDLETGVPSR ISGSGSGTDFTFITIS NLOPEDIATYYCQYD SLPLTFGGGKVEIRRTVAAPSVFIFPPSDEQ (SEQ ID NO: 34)
CDR1 CDR2 CDR3

FIG. 23

ACCATCACTT GCCAGGGCAG TCAGGACATA AGCACTATT TAAATTGGTA TCAGCAGAAA CCAGGGAAG CCCCT AAGCTCCIGA TCAACGATGC ATCCGATTG GAAACAGGGG
TCCCATCAAG GATCAGTGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAG CAACCTGCAG CCTGAAGATA TTGCAACATA TTACTGTCAA CAATATGATA GTCTC CCGCTCACTT
TCGGCGGAGG GACCAAGGTG GAGATCAGA (SEQ ID NO: 14)

FIG. 24

VS GGSV YSGDY YWSWIRPPKGLWIGYIYYSGSTNYPNPSLKS RVTISVDTSKNQFSLKLS SSVTAADTAVYYC ARDSILGATNYWG GGLTVTVSS (SEQ ID NO: 35)

CDR1

CDR2

CDR3

FIG. 25

GTCTCTGGTG GCTCCGCTCTA CAGTGGTGAT TACTACTGGA GCTGGATCCG GCAGCCCCCCC GGAAGGGAC TGGAGTGGAT TGGGTATATC TATTACAGTG GGAGCACCAC TTAACAATCCC
TCCCTCAAGA GTCGAGTCAC CATATCAGTA GACAGGTCCA AGAACCAAGT CTCCTGAAG CTGAGCTCTG TGACCGCTGC GGACACGGCC GTGTATTACT GTGCGAGAGA CTCACATAC TG
GGAGCTACCA ACTACTGGGG CCAGGGAACC CTGGTCACCG TCTCCTCA (SEQ ID NO: 15)

FIG. 26

TTTCQASD XISNYL XWYQKPKGKAPK XLI S DASNLETGVP SRFSGSGSGT XXIFTISSLPEDIAIYHcXQYXS LPLIFGGGTKVEIKRTVA RPSVFI PPSPDEQ (SEQ ID NO: 36)

CDR1

CDR2

CDR3

FIG. 27

ACCATCACTT GCCAGGGCAG TONGGACATT AATAACTATT TANATTGGTN TCAGCAGAAA CCAGGGAAG CCCCT AAATCCCTGA TCTCCGATGC ATCCAATTTA GAAACAGGGG
TCCCATCGAG GTTCAGTGA AGTGGATCTG GGACA GANTNTACTT TCACCATCAG CAGCCTGCAG CCTGAAGATA TTGCNACATA TCACTGTGCTA CAGTATNATA GTCTC CCGCTCACTT
TCGGCGGAGG GACCAAGGTA GAGATCAAA (SEQ ID NO: 16)

FIG. 28

VSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNNYNPSLKSRLLTISIDTSKTQFSLKLSVTAADTAJYCVRDRVTGAFDIVGGGTMTVSS (SEQ ID NO: 37)

CDR1 CDR2 CDR3

FIG. 29

GTCTCTGGTG GCTCCGTCAG CAGTGGTGAT TACTACTGGA CTTGGATCCG GCAGTCCCA GGAAGGGAC TGGAGTGGAT TGGACACATC TATTACAGTG GGAACACCAA TTATAACCCC
 TCCCTCAAGA GTGACTCAC CATATCAATT GACAGTCCA AGACTCAGTT CTCCTGAAG CTGAGTTCTG TGACCGCTGC GGACACGGCC ATTATTACT GTGTGGGAGA TCGAGTGACT
 GGTGCTTTTG ATATCTGGG CCAAGGGACAATGGTCACCG TCTCTTCA (SEQ ID NO: 17)

FIG. 30

TTTCQASQDISNYLNYQQKPKAPKLLIYDASNLETVPSRFSGSGSGTDFTFITSSLOPEDIAITYFCQHF^DHLPLAFGGGKVEIKRTVAAPSVFIPPPSDEQ (SEQ ID NO: 38)

CDR1 CDR2 CDR3

FIG. 31

ACCATCACTT GCCAGGCGAG TCAGGACATC AGCACTATT TAAATTGGTA TCAGCAGAAA CCAGGGAAG CCCCT AAATCCTCGA TCTACGATGC ATCCAATTG GAAACAGGGG
 TCCCATCAG GTTCAGTGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAG CAGCCTGCAG CCTGAAGATA TTGCAACATA TTCTGTCAA CACTTTGATC ATCTC CCCTCGCTT
 TCGGCGGAGG GACCAAGGTG GAGATCAAA (SEQ ID NO: 18)

FIG. 32

Amino Acid Sequences and Structure of Human Heavy Chain Derived from EGFR-Specific Hybridomas

Human $\gamma 2$	CDR1	CDR2	CDR3	ASTKGPSVFPLAPCSRSTST (SEQ ID NO: 19)
4-31	VSGGSSGGYYWSMIRQHPGKGLEWIGYIYYSGSTYNPNP	SLKSRVTISVDTSKNQFSLKSSVTAADTAVYYCAR	STVWNP	WFDPP (SEQ ID NO: 42)
E1.1	N-D	DC	F-T	VGQGLVTVSS (SEQ ID NO: 43)
E2.4	N-D	S-N-F	L	VGQGTWTVSS (SEQ ID NO: 44)
E2.5	D-T	N	SM-I-E	VGQGLTVTVSS (SEQ ID NO: 45)
E6.2	N-DF	M-I-P	TSLYYGG	GMDV (SEQ ID NO: 46)
E6.4	NN-D	I	GTVTYY	YFDY (SEQ ID NO: 47)

CDR1	CDR2	CDR3	(SEQ ID NO: 22)
4-61	VSGGSVSSGYYWSMIRQPPGKGLEWIGYIYYSGSTYNPNP	SLKSRVTISVDTSKNQFSLKSSVTAADTAVYYCAR	DFLIGSF FDY (SEQ ID NO: 47)
E2.11	D	HL-N	VGQGTWTVSS (SEQ ID NO: 48)
E6.3	Y-D	DSILGA	TNY (SEQ ID NO: 49)
E7.6.3	D-T	S-N	VGQGTWTVSS (SEQ ID NO: 49)

FIG. 33

Amino Acid Sequence and Structure of Human Kappa Chain Derived from EGFR-Specific Hybridomas

	V _K SEGMENT			J _K SEGMENT	
	CDR1	CDR2		CDR3	
V _K (018)	TITQASQDTSNYLN	NYQQKPGKAPKLLIYDASNLEIGVPSRFGSGSGTDFTFITISLQPEDIAITYYQQQYDNL		RTVAAPSVFIFPPSDEQ	(SEQ ID NO: 41)
Human Ck					(SEQ ID NO: 20)
EGF.1.1.K	N--F--N--	V--H--G--		LTGGGKVEIK	(SEQ ID NO: 24)
EGF.2.4.K	TI--N--S--L--	N--S--L--		LTGGGKVAIK	(SEQ ID NO: 26)
EGF.2.5.K			VG--V--ES--	CGGGGKLEIK	(SEQ ID NO: 28)
EGF.2.11.K		N--D--I--	N--N--	LTGGGKVEIR	(SEQ ID NO: 34)
E6.2.K	N--R--N--	R--N--	H--H--	VTGGGKVEK	(SEQ ID NO: 30)
E6.3.K	X--N--X--	X--S--	H--X--XS--	LTGGGKVEIK	(SEQ ID NO: 36)
E6.4.K*	R--S--S--	A--S--QS--	GYRT-PE	CSGGGKLEIK	(SEQ ID NO: 32)
*012 Gene 21			F--F--HF--H--	LAFGGKVEIK	(SEQ ID NO: 38)
E7.6.3.K					

FIG. 34

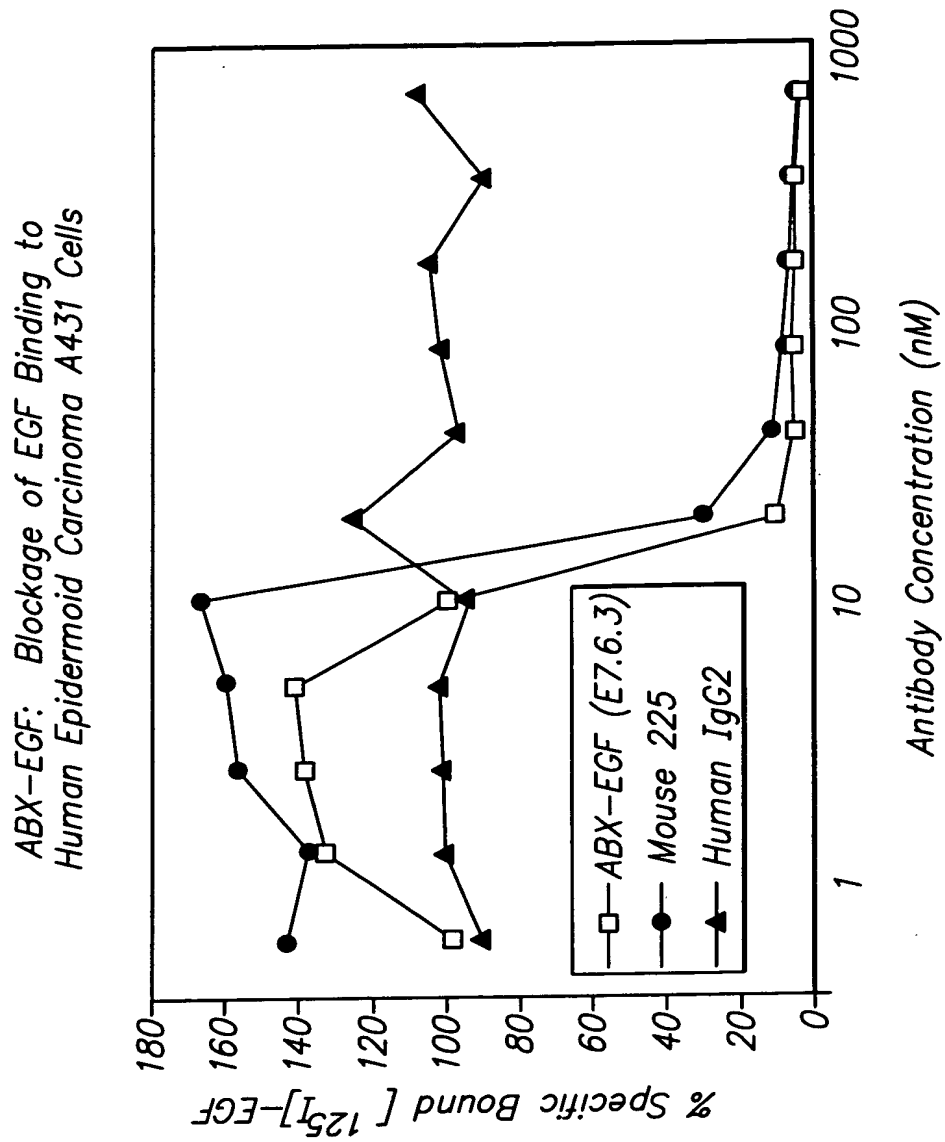
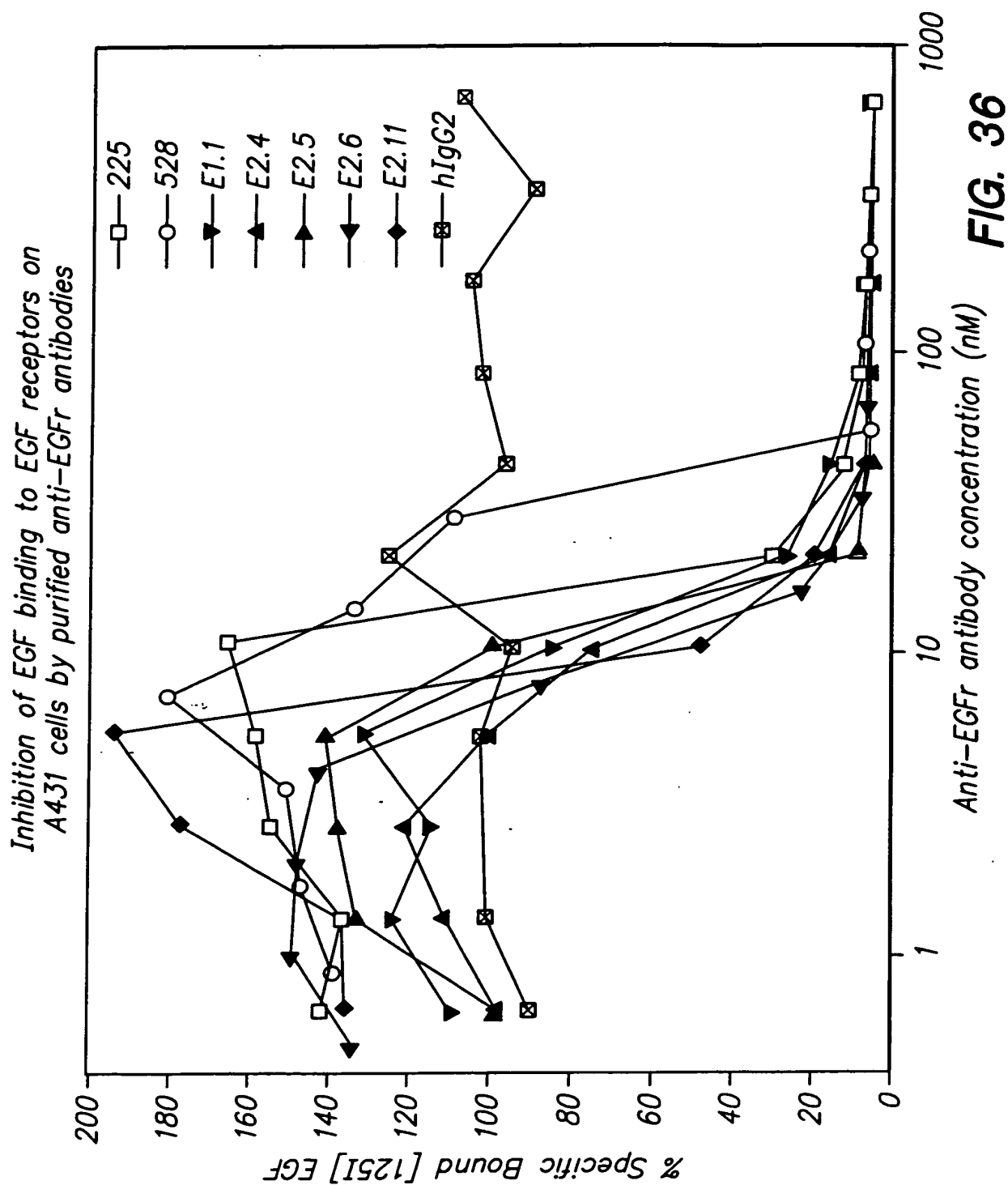


FIG. 35



*Inhibition of TGF- α binding to A431 cells
 by anti-EGF receptor antibodies*

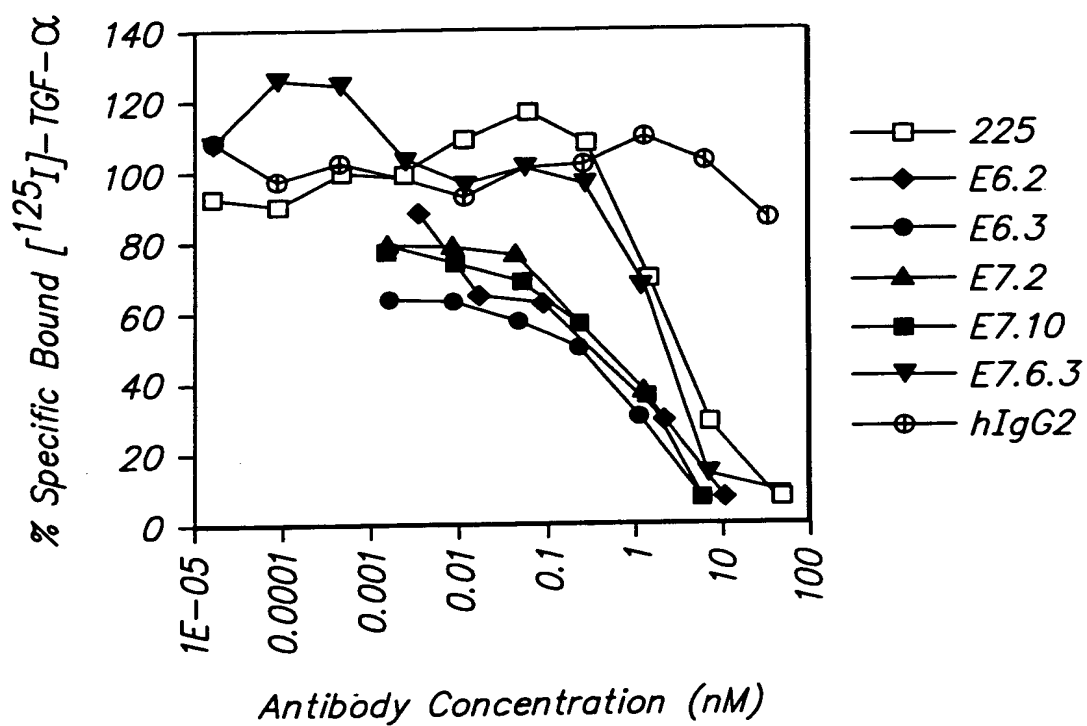


FIG. 37

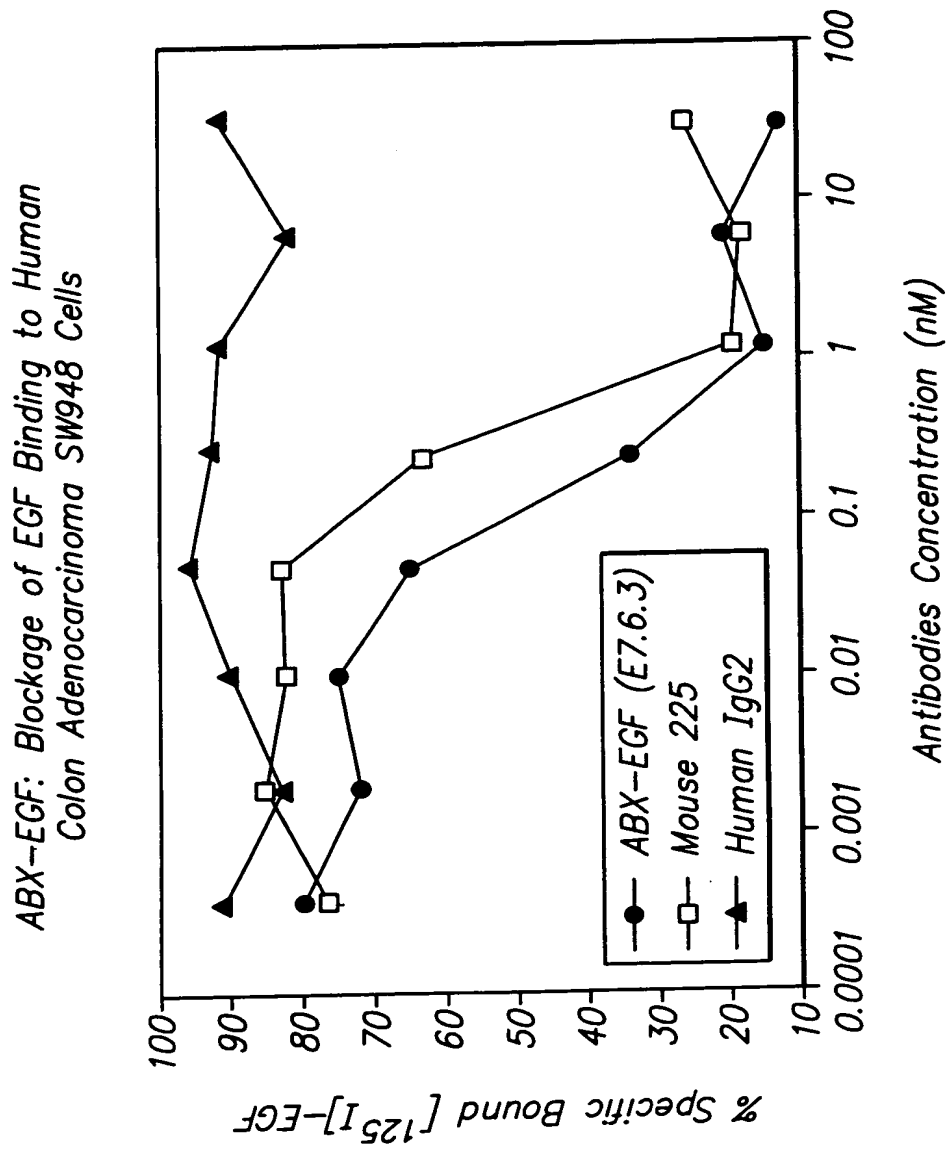


FIG. 38

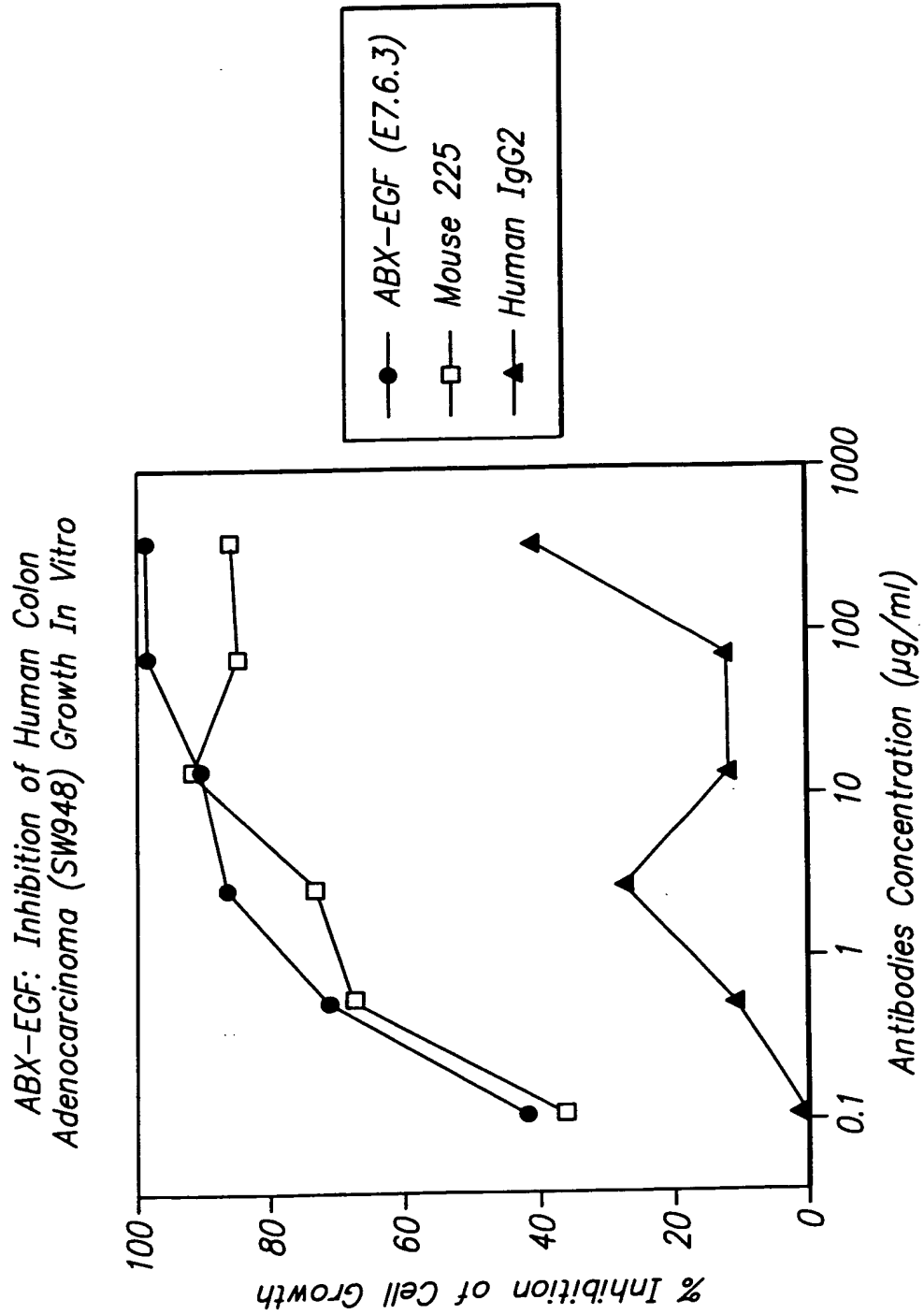


FIG. 39

ABX-EGF: Inhibition of Human Epidermoid
 Carcinoma Growth in Nude Mice

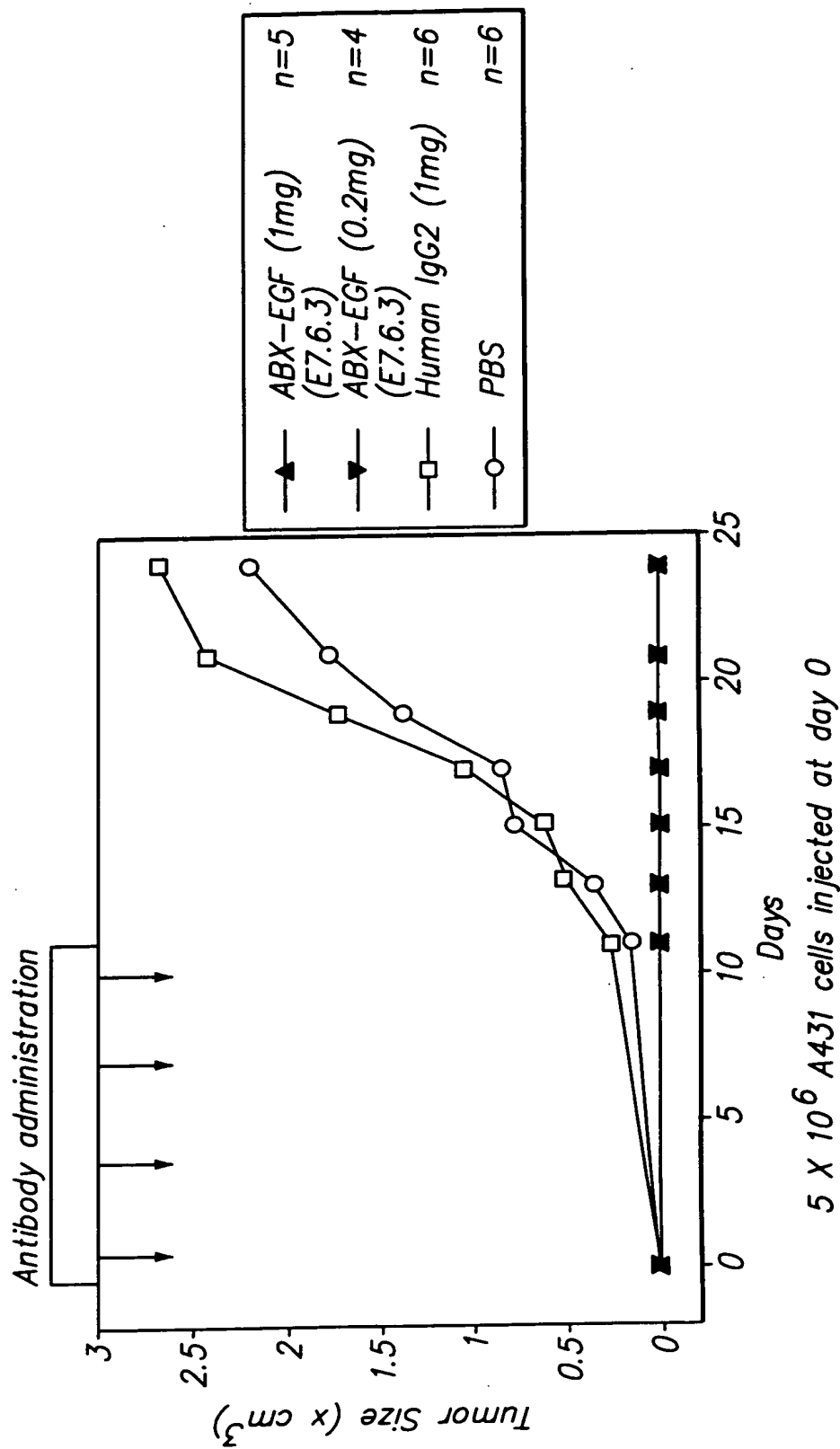


FIG. 40

*Inhibition of Human Epidermoid Carcinoma
 Formation in Nude Mice by ABX-EGF*

<i>Treatment</i>	<i>Dose (mg)</i>	<i>Tumor Formation^b (incidence)</i>	<i>Tumor size^c (cm³)</i>
PBS		6/6	1.376
Human IgG2 ^a	1	6/6	1.727
E7.6.3	1	0/5	0
	0.2	0/4	0
E2.5	1	0/3	0
	0.2	0/3	0
E1.1	1	0/3	0

^a control human myeloma IgG2

^b incidence determined 19 days post tumor inoculation

^c tumor size measured 19 days post tumor inoculation

FIG. 41

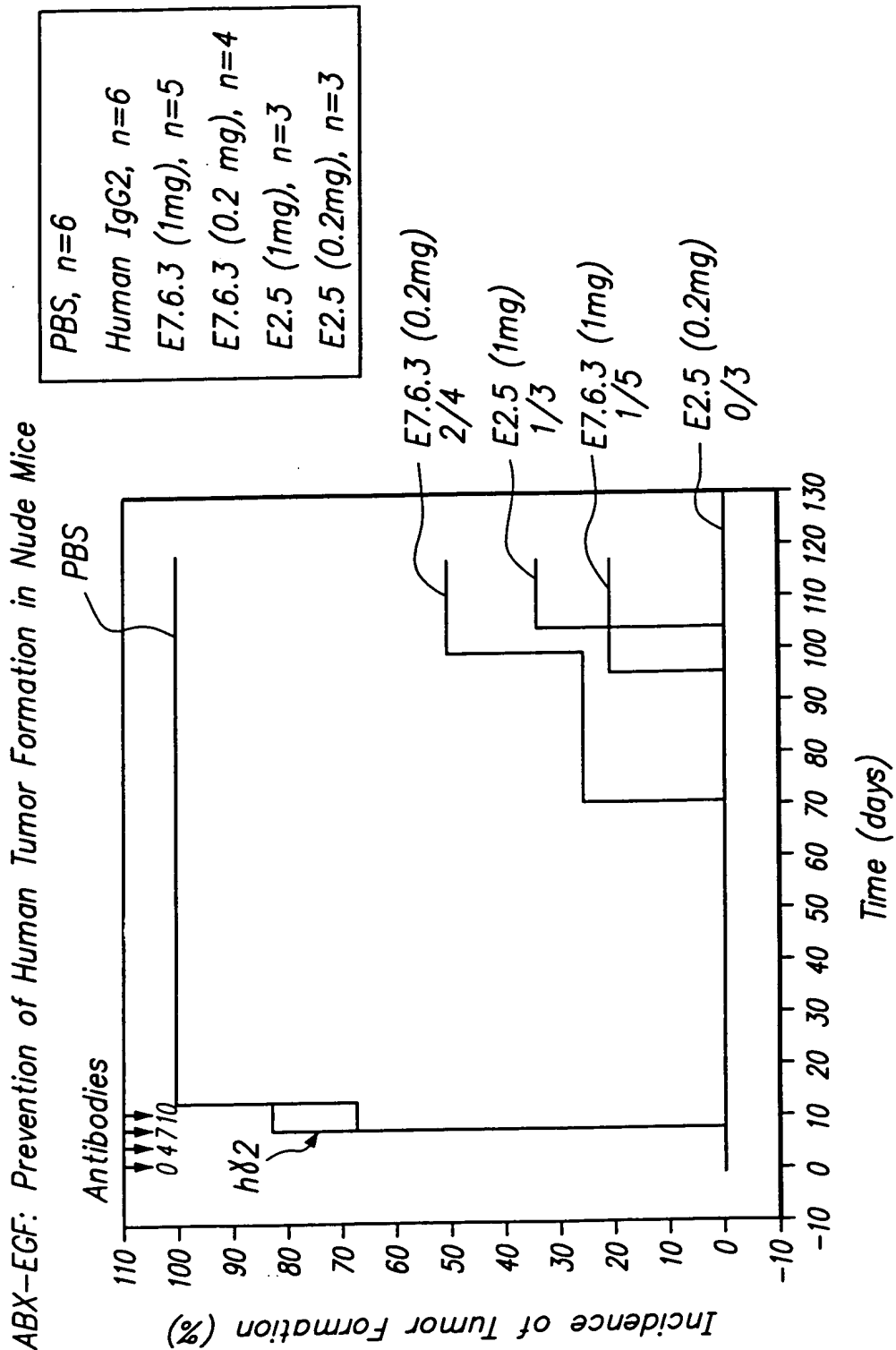


FIG. 42

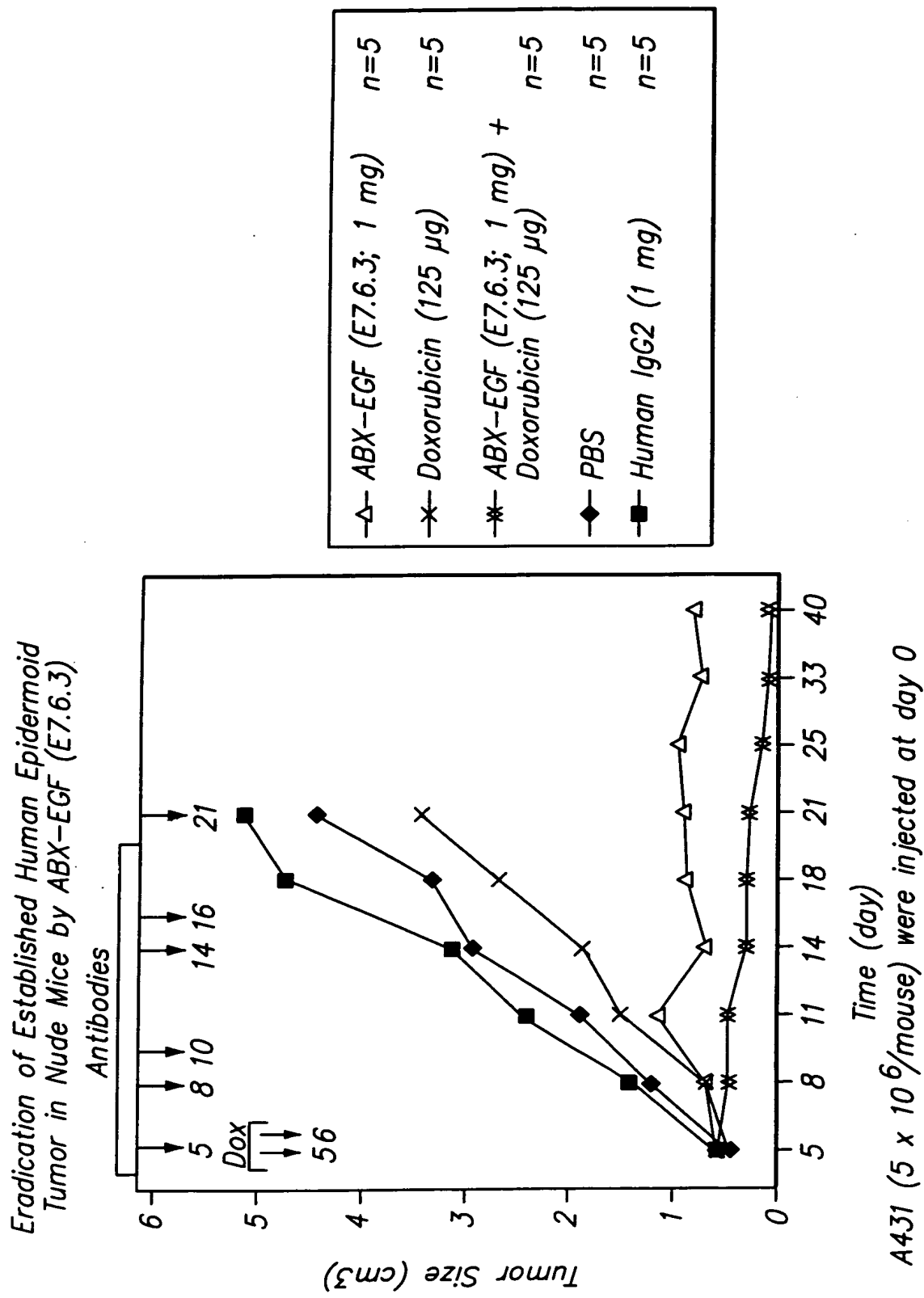


FIG. 43

Eradication of Established Human Epidermoid
 Tumor in Nude Mice by ABX-EGF (E2.5)

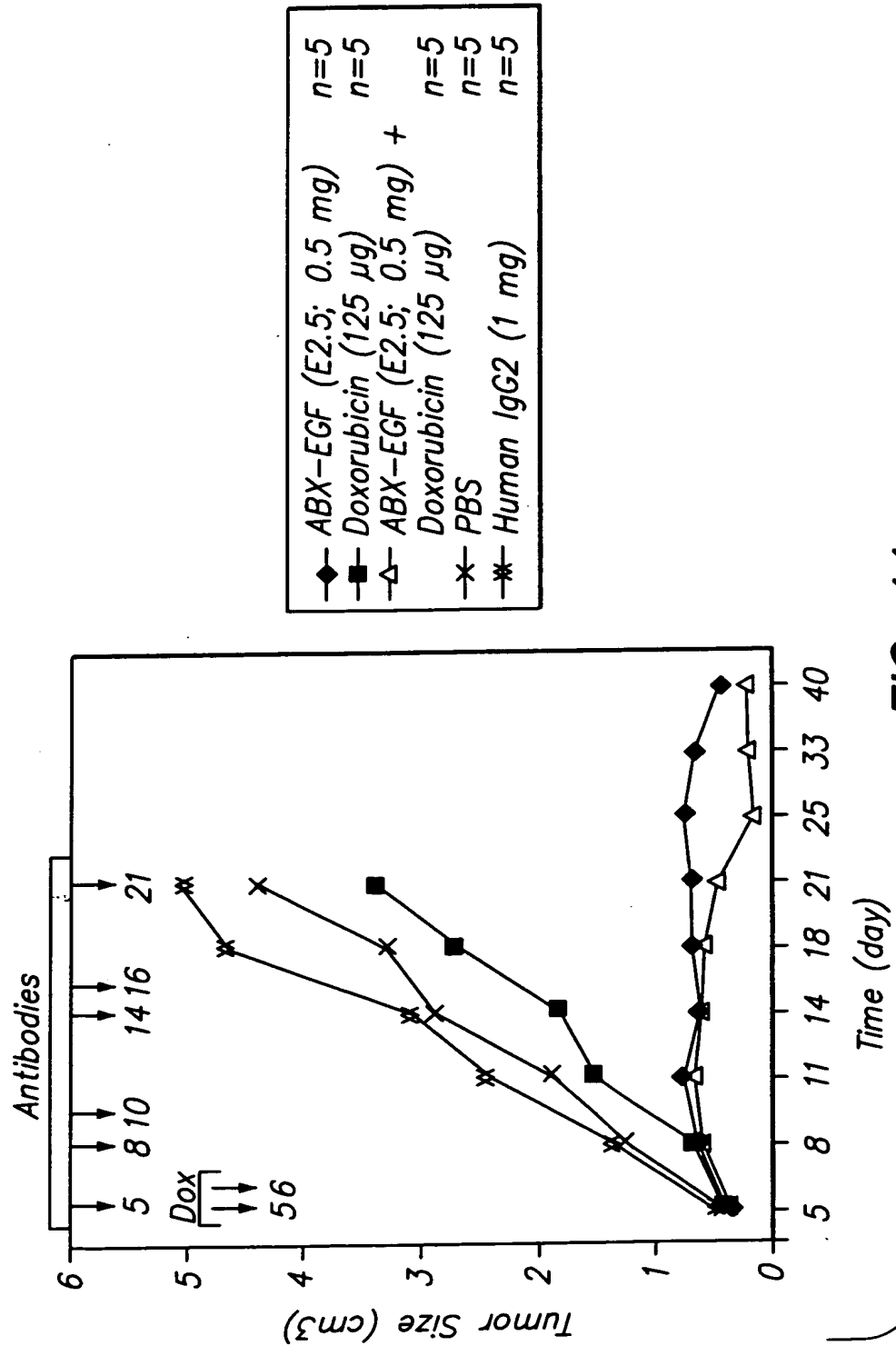


FIG. 44

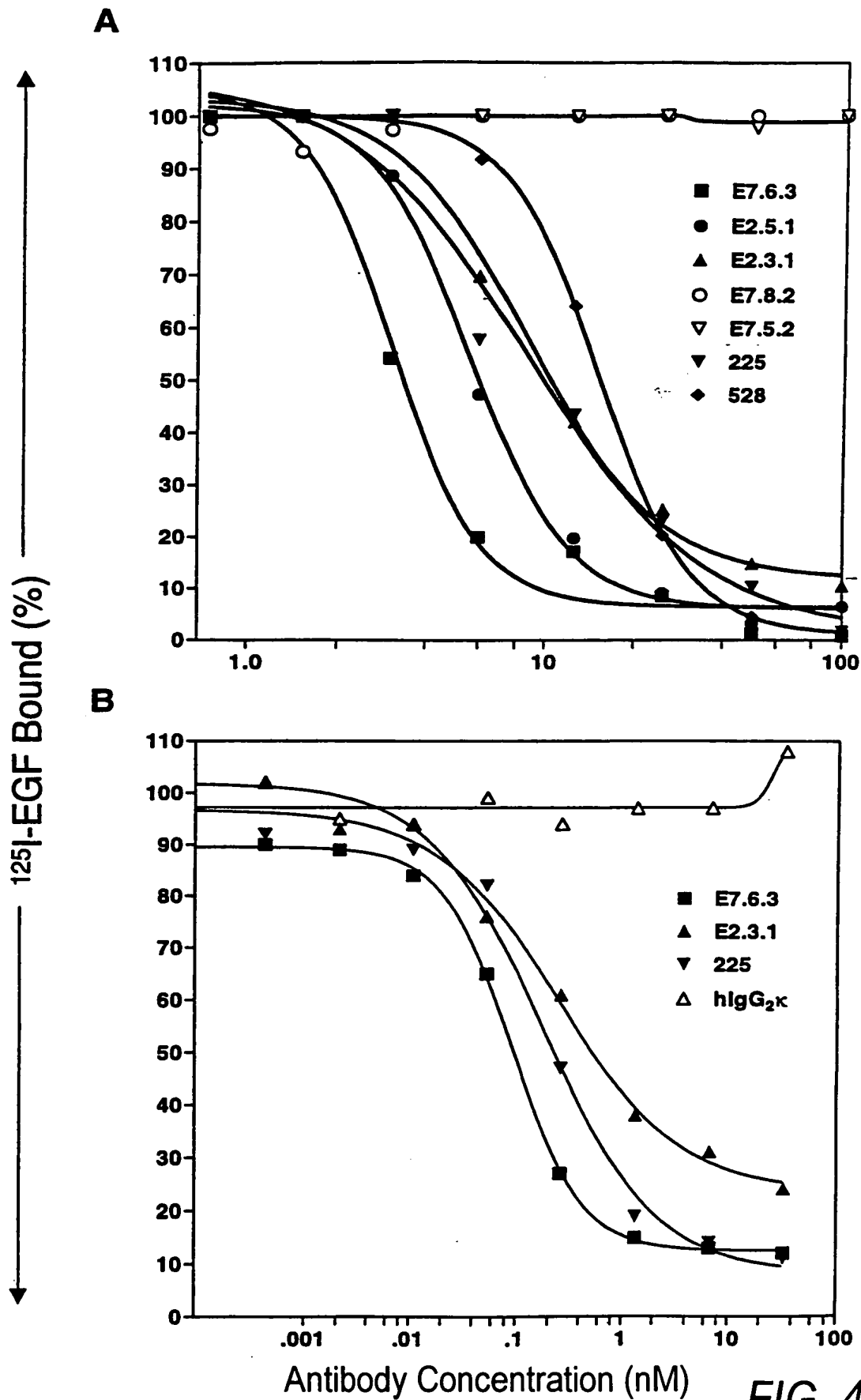


FIG. 45

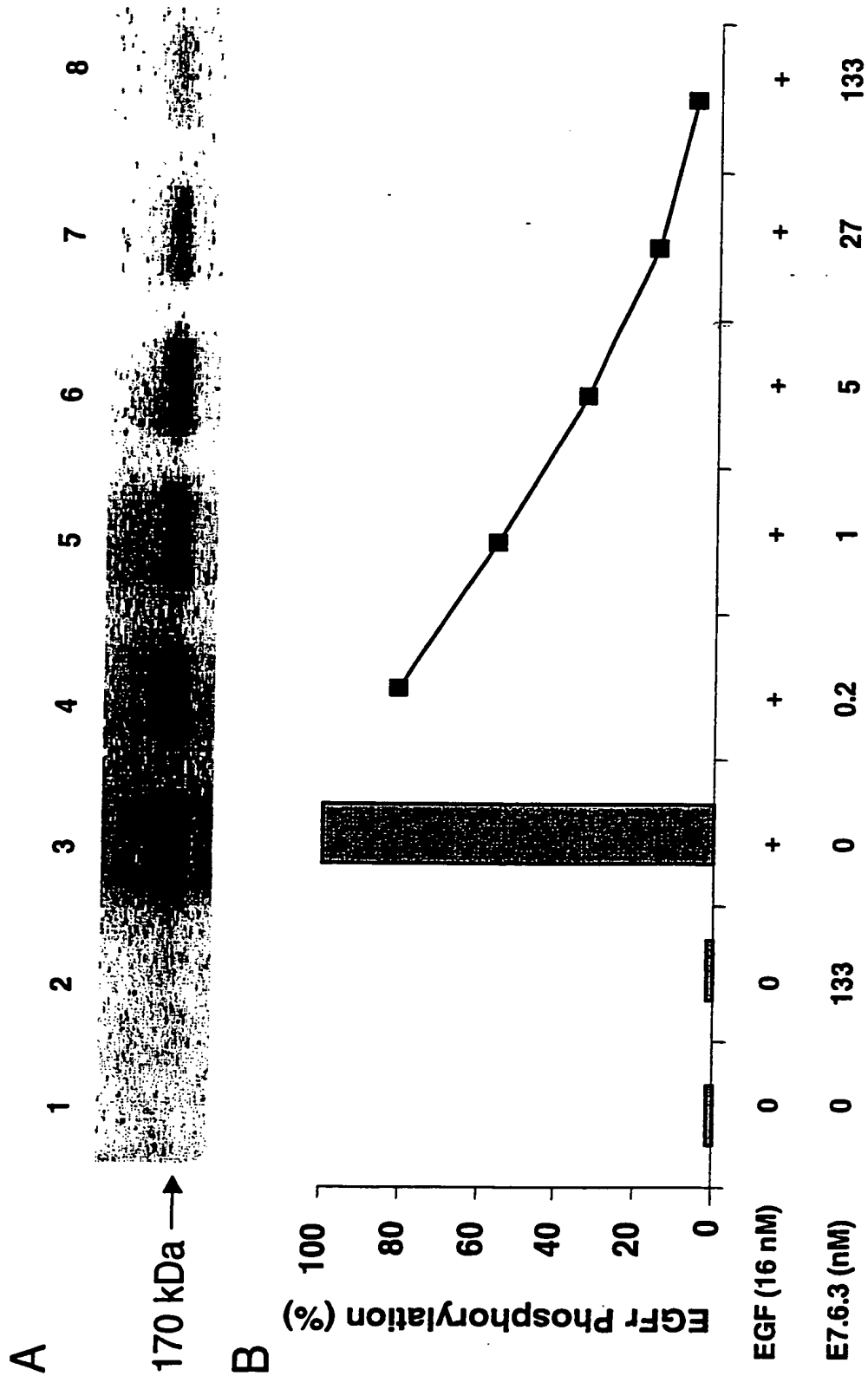
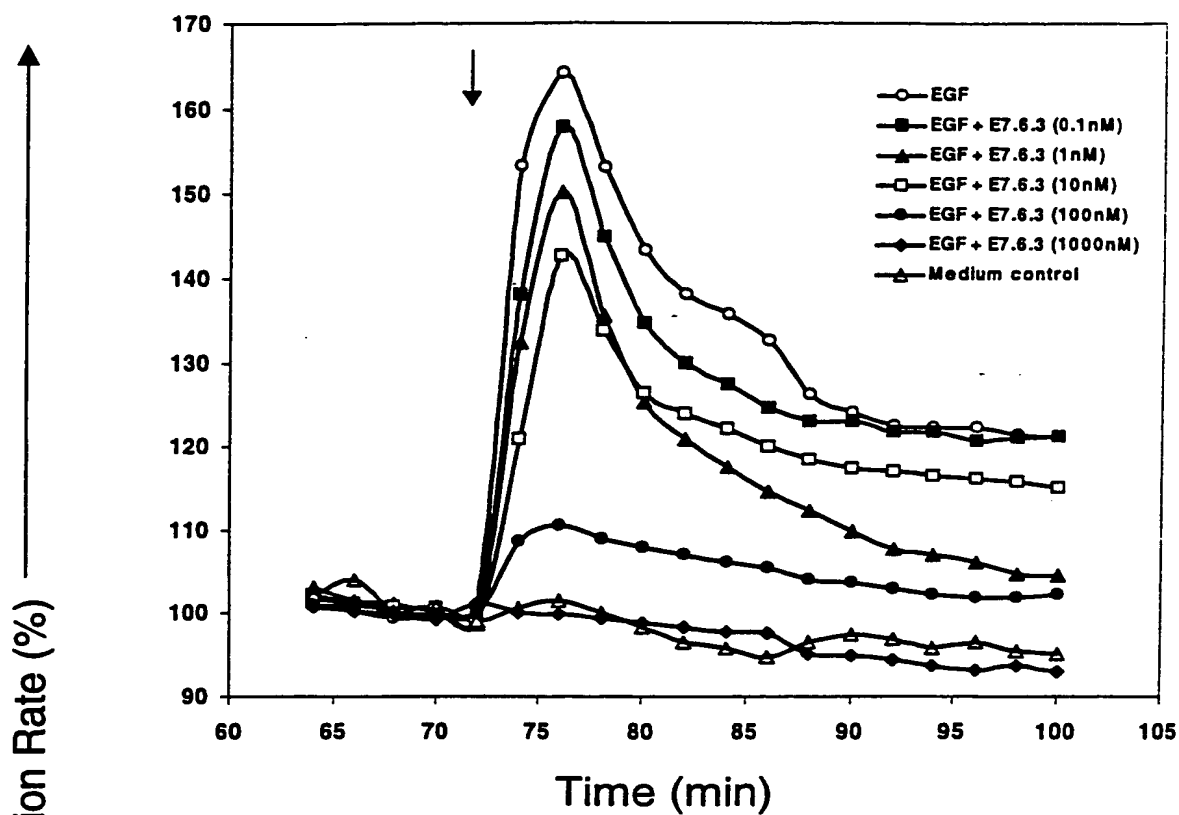


FIG. 46

A



B

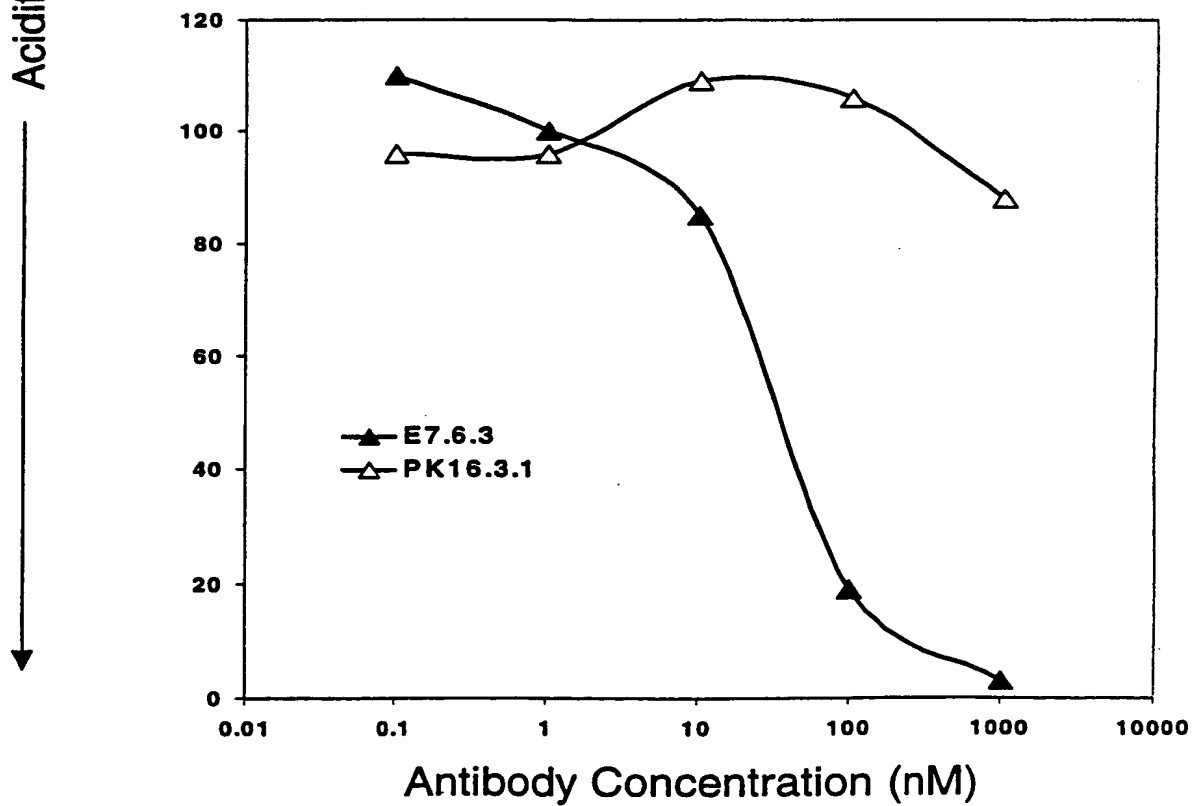
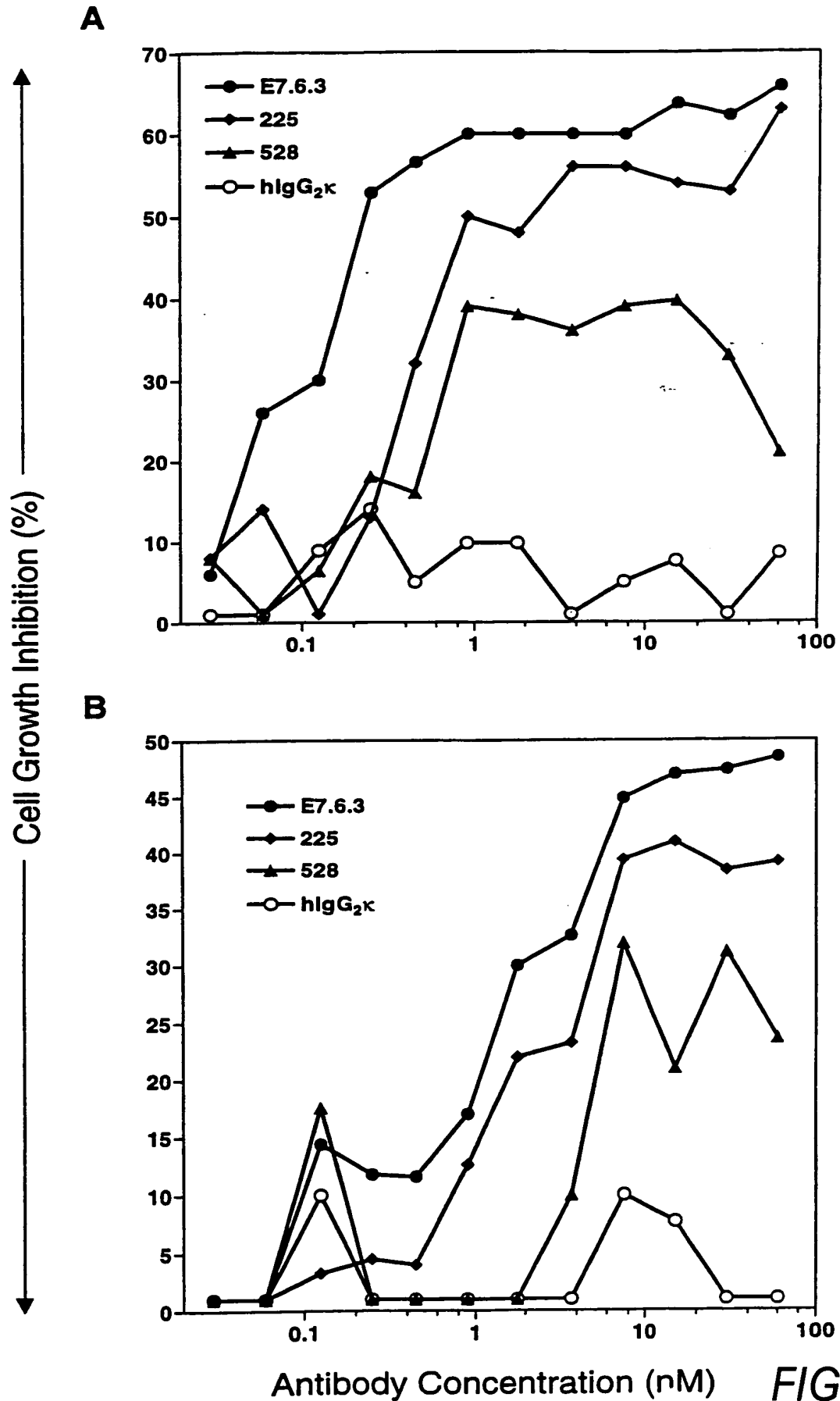


FIG. 47



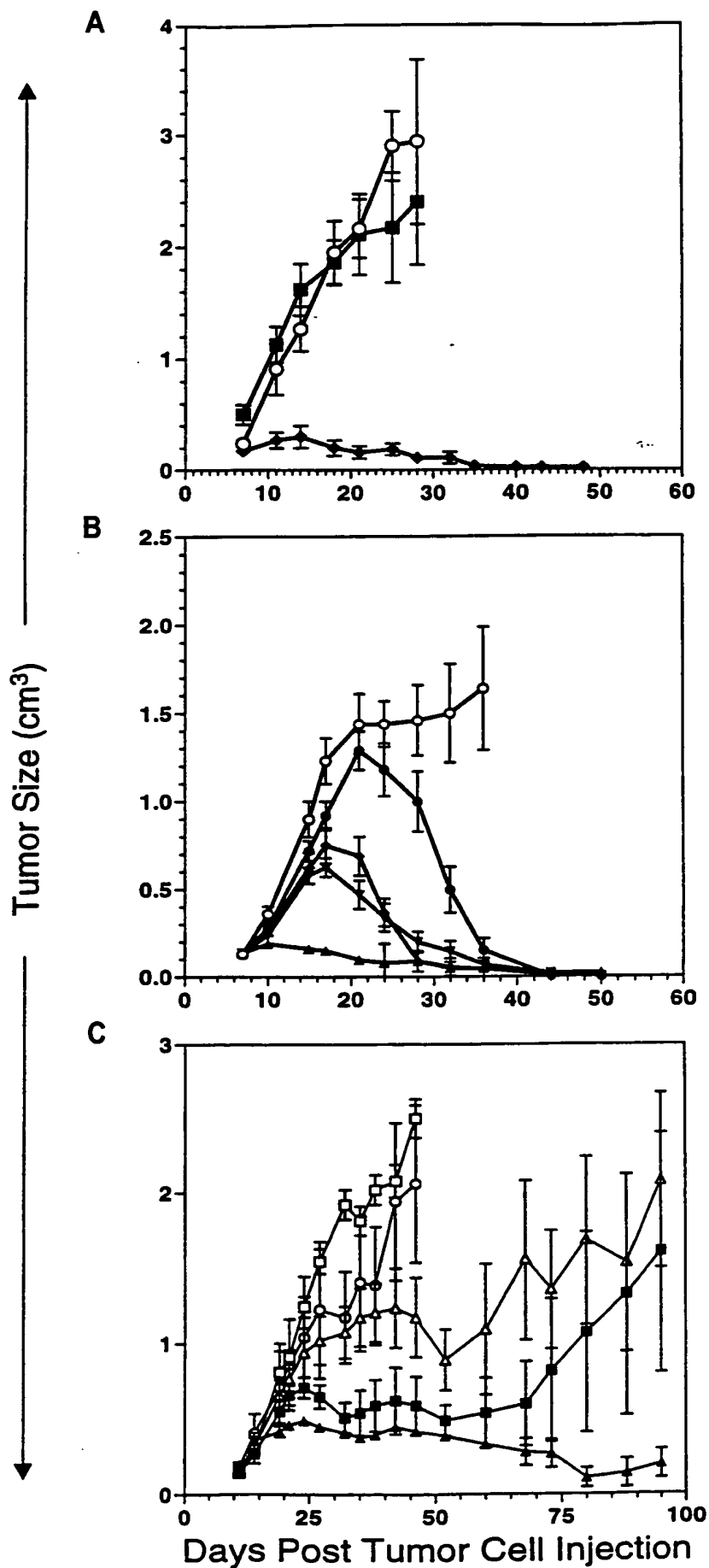


FIG. 49

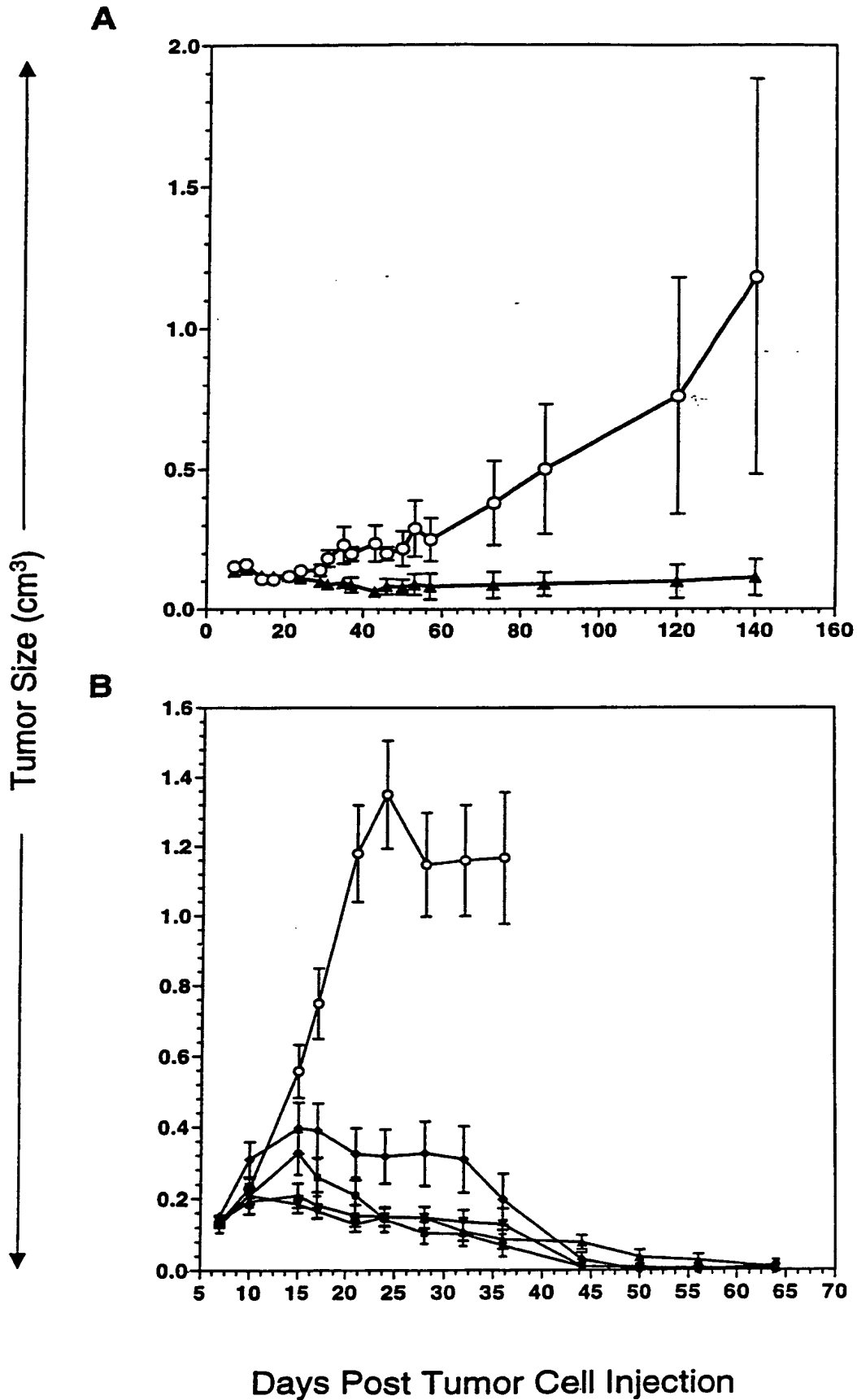


FIG. 50

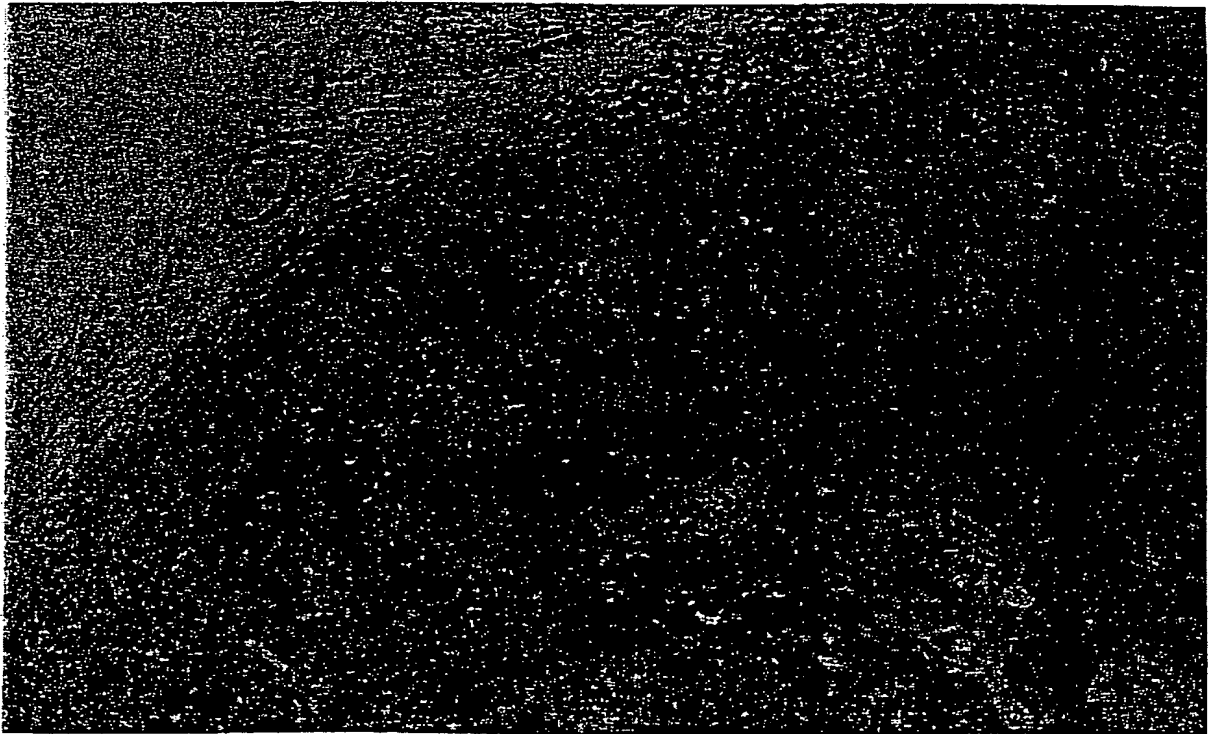


FIG. 51

Time (day)	Incidence of Tumor Formation		
	PBS	PK16.3.1 (1 mg)	E7.6.3 (0.2 mg) E7.6.3 (1 mg)
0	0/5	0/5	0/10
3	4/5	0/5	0/10
8	4/5	3/5	0/10
10	5/5	5/5	0/10
25	5/5	5/5	0/10
100	ND	ND	0/10
250	ND	ND	0/10

FIG. 52

Tumor-free Mice on Day 60			
Treatment (dose/injection)	Total Dose	Total No. of Mice	%
None		71	0
Control IgG ₂ κ (1 mg)	6 mg	16	0
E7.6.3 (1 mg)	6 mg	50	100
E7.6.3 (0.5 mg)	3 mg	20	95
E7.6.3 (0.25 mg)	1.5 mg	5	60
E7.6.3 (0.2 mg)	1.2 mg	19	26
E7.6.3 (0.1 mg)	0.6 mg	20	65
E7.6.3 (0.05 mg)	0.3 mg	15	7

FIG. 53

Inhibitory Effects of E7.6.3 on EGF-induced Tyrosine-phosphorylation and Degradation of EGFr in Cultured A431 Cells

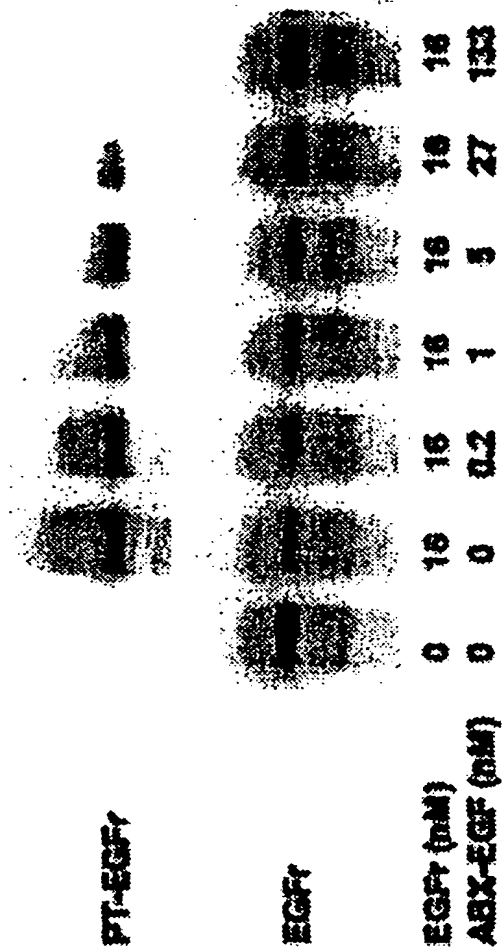


FIG. 54

Preliminary results obtained comparing Inhibitory Effects of E 7.6.3 and 225 on EGF-induced Tyrosine-phosphorylation and Degradation of EGFr in Cultured A431 Cells



Preliminary results obtained comparing
 Effects of EGF, ABX-EGF and 225 on
 Tyrosine-phosphorylation and Degradation of EGFr in
 Cultured A431 Cells

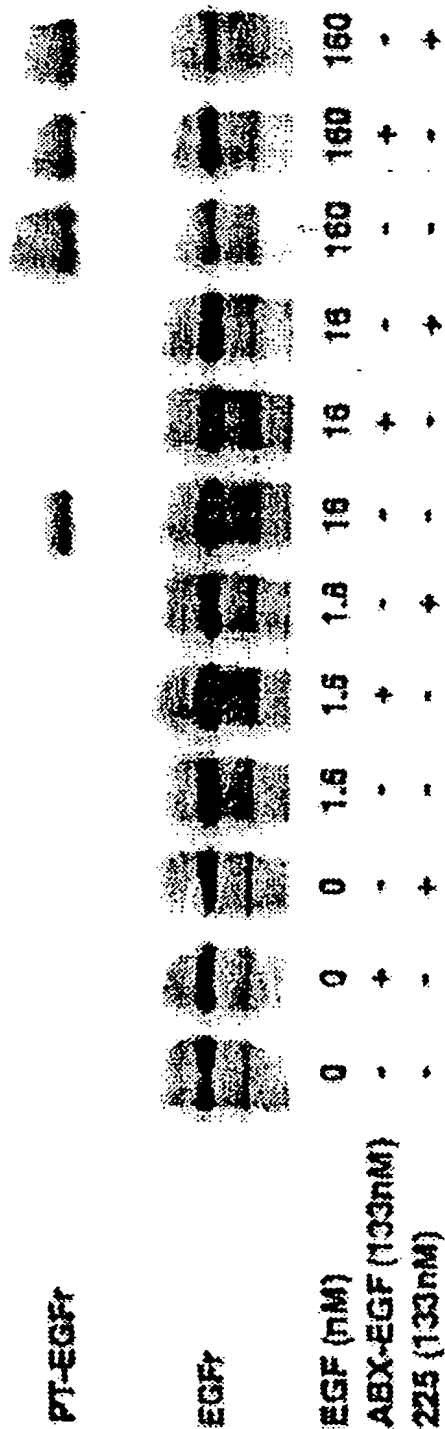


FIG. 56

E20.1MG30.Seq Sequ nce

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
GCGATCCAGC	CTTTTAGGTC	CATGCGNTTC	TCTGTGNAG	CGTCTGGATT	50
A I Q P	F R S	M P F	S C X A	S G F	
CCCCITCAGT	AGNINIGGCA	TGCACTGGGT	CCGCCAGGCT	CCAGGCAAGG	100
P F S	X X G M	H W V	R Q A	P G K G	
GGCTGGAGTG	GGTGGCAGTT	ATATGGIATG	ATGGAAGTAA	TAAATACTAT	150
L E W	V A V	I W Y D	G S N	K Y Y	
GCAGACTCCG	TGAAGGGCCG	ATTCACCATC	TCCAGAGACA	ATTCCAAGAA	200
A D S V	K G R	F T I	S R D N	S K N	
CAOGCTGIAT	CTGCAAATGA	ACAGACTGAG	AGCGAGGAC	ACGGCTGTGT	250
T L Y	L Q M N	R L R	A E D	T A V Y	
ATTACTGIGC	GACATTTTTC	GAGTGGTTC	AGGCTGCTTC	AGGCTGCTTC	300
Y C A	R F L	E W L P	F D Y	W G Q	
GGTGGTGGT	GGTGGTGGT	GGTGGTGGT	GGTGGTGGT	GGTGGTGGT	350
G T L V	T V X	S D S	T K G P	S V F	
CNCCCTGGCG	CCCTGCTTCC	AGGAGCACCC	TGNGANAGCA	CANANGGCC	400
X L A	P C F Q	E H P	X X A	X X A P	
CTGGGACTGN	CTGNTACAAG	GACTINCTTTC	CCTCNAAACN	GGTGACCNIN	450
G T X	X Y K	D X F P	S N X	V T X	
TCNTGGGAAA	CTCAGNGCNC	NICTINNATNA	C	(SEQ ID NO: 19)	481
S W E T	Q X X	S X X		(SEQ ID NO: 55)	

FIG. 57

E20.1VK.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
GGAACTTTIN	GGTTCGNC	TTTTGGAGNC	AGACCCANCA	TCACITGTCTG	50
G T F X	F A P	F G X	R P X I	T C R	
GGCGAGTCAG	GGCATTAGCA	ATTTTTTAGC	CTGGTTTCAG	CAGAAACCAG	100
A S Q	G I S N	F L A	W F Q	Q K P G	
GGATAGCCCC	TAAGTCCCIG	ATCTATGCTG	CATCCACTTT	GCAAAGTGGG	150
I A P	K S L	I Y A A	S T L	Q S G	
GTCACATCAA	AGTTCACCGG	CAGTGGATAT	GGACAGATT	TCACTCTCAC	200
V P S K	F T G	S G Y	G T D F	T L T	
CATCAGCAGC	CTGCAGCCTG	AAGACTTTGC	AACTTATTAT	TGTCACAAT	250
I S S	L Q P E	D F A	T Y Y	C Q Q Y	
ATAATGTTTA	CCCATTCACT	TTCCGCCCCTG	GGACCAAAGT	GGATATCAAA	300
N V Y	P F T	F G P G	T K V	D I K	
CGAACTGIGG	CTGCACCATC	TGTCCTTCATC	TTCCCGCCAT	CTGATGAGCC	350
R T V A	A P S	V F I	F P P S	D E P	
AGTTGAAATC	TGGAACTGCC	TCTGTGTGIGT	GCCTGCTGAA	TAACTTCTAT	400
V E I	W N C L	C C V	P A E	L L S	
CCCAGACAGG	CCAAAGTACA	GTCGAAGGTG	GATAACGCCN	CNNITGGCGG	450
Q R G	Q S T	V E G G	R X	X W R	
NNTCCTTTN	CTCNCCTC	CTCNCCTC	CTCTCNCNA	(SEQ ID NO: 20)	489
X P F X	X P S	S X X	L S X	(SEQ ID NO: 56)	

FIG. 58

E20.3MG30.Seq S quence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
AAGCCIGTGTG	CCTCAGTGA	GGTCTCTGC	AAGGCTTCTG	GATACACCTT	50
K P V A	S V Q	V S C	K A S G	Y T F	
CACCAGTTAT	GATATCAACT	GGGTGGGACA	GGCCACTGGA	CAAGGGCTTG	100
T S Y	D I N W	V R Q	A T G	Q G L E	
AGTGGATGGG	ATGGATGAAC	CCTAACAGTG	GTAACACAGG	CTATGCACAG	150
W M G	W M N	P N S G	N T G	Y A Q	
AAGTTCCAGG	GCAGAGTCAC	CATGACCAGG	AACACCTCCA	TAAGCACAGC	200
K F Q G	R V T	M T R	N T S I	S T A	
CTACATGGAG	CTGAGCAGCC	TGAGATCTGA	GGACACGGCC	GTGTATTACT	250
Y M E	L S S L	R S E	D T A	V Y Y C	
DNI					
GTGGCAGAGG	AGGCCCCAT	AGCAGTGGCT	GGACCTTCTT	TGACTACTGG	300
A R G	G P Y	S S G W	T F F	D Y W	
GGCCAGGGAA	CCCTGGTCAC	CGTCTCTCA	GGCTTNCACC	AAGGGCCCAT	350
G Q G T	L V T V	S S	A L H Q	G P I	
CGGTCCTCCC	CCTGGCGCCC	TGCTCCAGGA	GCACTTCCCA	GAGCACANIC	400
G L P	P G A L	L Q E	H L P	E H X X	
NNCCCTTGGG	CTGCCCTGGNN	CAAGGACTCT	TTCCCCNAAC	CCCGGNTGA	(SEQ ID NO: 21) 449
P L G	C L X	Q G L F	P X T	P X	(SEQ ID NO: 57)

FIG. 59

E20.3VK.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
TTTGAACCT	TCTGGGCGT	GTCTCTGGC	GCGAGGGCA	CCATCAACTG	50
F E P F	X A V	S L G	A R A T	I N C	
CAAGTCCAGC	CAGCGTGTTT	TATACANCTC	CAACAATAAG	AACTGCTTAG	100
K S S	Q R V L	Y X S	N N K	N C L A	
CTTGGTACCA	GCAGAAACCA	GGACAGCCTC	CTAAGCTGCT	CATTTACTGG	150
W Y Q	Q K P	G Q P P	K L L	I Y W	
ACATCTACCC	GGGAATCCGG	GGTCCCCTGCC	CGATTTCAGTG	GCAGCGGGTC	200
T S T R	E S G	V P A	R F S G	S G S	
TGGGACAGAT	TTCACTCTCA	CCATCAGCAG	CCTGCAGGCT	GAAGATGTTG	250
G T D	F T L T	I S S	L Q A	E D V A	
CAGTTTATTA	CTGTACAGCA	TATTATAGTA	CTCCACTCAC	TTTCGGGGGA	300
V Y Y	C Q Q	Y Y S T	P L T	F G G	
GGGACCATGG	TGGAGATCAA	GCGAAGTGIG	GCTGCACCAT	CTGTCTTCAT	350
G T M V	E I K	R T V	A A P S	V F I	
CTTCCCAGCA	TCTGATGAGC	CNGINIGAAA	TCTGGAACTG	CCTCTGTTTG	400
F P P	S D E P	V	N L E L	P L F V	
TGTGCCCTGC	TGAATAACTT	CTATCCCAGA	GAGGCCAAAG	TACCAGTGG	450
C P A	E	L L S Q R	G Q S	T S G	
AGGTTGATAA	(SEQ ID NO: 22)				460
R W I	(SEQ ID NO: 58)				

FIG. 60

E20.8.1MG30.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
CNGCCTGTGA	GGTCNIGCG	ACTCTCCTGT	GCAGCGTCTG	GATTCATCTT	50
X P V R	S X R	L S C	A A S G	F I F	
CAGTAGNIAT	GGCATGCACT	GGGTCCGCCA	GGCTCCAGGC	AAGGGGCTGG	100
S X Y	G M H W	V R Q	A P G	K G L E	
AGTGGGTGGC	AATTATATGG	TATGATGCCA	GTAATAAATA	CTATGCAGAC	150
W V A	I I W	Y D G S	N K Y	Y A D	
TCGGTGAAGG	GOOGATTAC	CATCTCCAGA	GACAATTCCA	AGAACAAGCT	200
S V K G	R F T	I S R	D N S K	N T L	
GTATCTGCAA	ATGAACAGCC	TGAGAGCCCA	GGACAAGGCT	GIGTATTACT	250
Y L Q	M N S L	R A E	D T A	V Y Y C	
GTGCGAGAGA	CGGGGGGCCA	<u>CGGTTGTTTC</u>	TCGCTTCTGA	CTACTGGGGC	300
A R D	G G P	R W F L	A S D	Y W G	
CAGGCAACCC	TGGTCACCGT	CTCCTCAGCC	TCCACCAAGG	GOOCATCGGT	350
Q G T L	V T V	S S A	S T K G	P S V	
CTTCCCCCTG	GCGCCCTGCT	CCAGGAGCAC	OCTTCGAGAG	CACAGCGGCC	400
F P L	A P C S	R S T	L R E	H S G P	
CTGGGCTGOC	TGGTICAAGG	ACTACTTTCC	CCGAACCGGT	GACGGTGINC	450
G L P	G S R	T T F P	E P V	T V X	
GTGGAACTC	ATGAC	(SEQ ID NO: 23)			465
V G T H	D	(SEQ ID NO: 59)			

FIG. 61

E20.8.1MG18.Seq Sequ nc

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
AGTCTCCAGA	CTCCCTGGTT	GTGTCCTCTG	GCGAGAGGGC	CACCATCAAC	50
S L Q T	P W L	C L W	A R G P	P S T	
TGCAAGTCCA	GNCAGAGTAT	TTTATACAGC	TCCAACAATC	AAAAACTTCT	100
A S P	X R V F	Y T A	P T I	K N F L	
TAGCTTGGTA	CCAGCAGAAA	CCAGGACAGC	CTCCGAAGTT	GCTCATTTAC	150
A W Y	Q Q K	P G Q P	P K L	L I Y	
TGGGCATCTA	TTCCGGGAATC	CGGGGTCOCT	GACCGATTCA	GTTGGCAGCGG	200
W A S I	R E S	G V P	D R F S	G S G	
GTCTGGGACA	GATTTCACCTC	TCACCATCAG	CAGCCTGCAG	GCTGAAGATG	250
S G T	D F T L	T I S	S L Q	A E D V	
TGGCAGTTTA	TTACTGTTCAG	CAGTATTATA	GIATTCCGTG	CACTTTIGGC	300
A V Y	Y C Q	Q Y Y S	I P C	T F G	
CAGGGGACCA	AGCTGGAGAT	CAAACGAAC	GTTGGCTGCAC	CATCTGTCTT	350
Q G T K	L E I	K R T	V A A P	S V F	
CATCTTCCCG	CCATCTGATG	AGCAGTTGAA	ATCTGGAACT	GCCTCTGTG	400
I F P	P S D E	Q L K	S G T	A S V V	
TGIGCCTGCT	GAATAACTTC	TATCCCAGAA	AGGCCAAAGT	ACATGAAGGG	450
C L L	N N F	Y P R K	A K V	H E G	
TTCAAA	(SEQ ID NO: 24)				456
F K	(SEQ ID NO: 60)				

FIG. 62

E20.11.2H Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
GGCGTGGYCC	AGCCTGKAG	GTCCTGAGA	CCTCCTGTG	CAGCGTCTGG	50
G V X Q	P X R	S L R	L S C A	A S G	
ATTCAVCTTC	AGTARCTATG	GCATGCACTG	GGTCGCGCAG	GCTCCAGGCA	100
F X F	S X Y G	M H W	V R Q	A P G K	
AGGGGCTGGA	GTTGGTGGCA	ATTATATGGT	ATGATGCAAG	TAGCAAATAC	150
G L E	W V A	I I W Y	D G S	S K Y	
TATGCAGACT	CCGTGAAGGG	CCGATTCAAC	ATCTCCAGAG	ACAATTCCAA	200
Y A D S	V K G	R F T	I S R D	N S K	
GAACAGCTG	TATCTGCAA	TGAACAGCCT	GAGAGCGCAG	GACACGGCTG	250
N T L	Y L Q M	N S L	R A E	D T A V	
TGTATTACTG	TGCGAGAGAC	GGGGGGGCAC	GGTGGTTTCT	CGCTTCTGAC	300
Y Y C	A R D	G G P R	W F L	A S D	
TACTGGGGCC	AGGGTACCT	GGTCACCGTC	TCTCAGCCT	CCACCAAGGG	350
Y W G Q	G T L	V T V	S S A S	T K G	
CCCATCGGTC	TTCCCCCTGG	CGCCTGCTC	CAGGAGCACC	TTCCGAGAGC	400
P S V	F P L A	P C S	R S T	F R E H	
ACAGCGGCCC	TGGGCTGCCT	GGTCAAGGAC	TACTTCCCCG	AAMCGGTGAC	450
S G P	G L P	G Q G L	L P R	X G D	
GGGTGCTGG	AACTCAGGCG	CTCTGACCAG	NGGCGTGCAC	AATTCCCAGC	500
G V V E	L R R	S D Q	X R A Q	F P A	
NGTCCINAAG	GTIGAAATCG	TAANGGTICA	AA	(SEQ ID NO: 25)	532
V L K	V E I V	X V Q		(SEQ ID NO: 61)	

FIG. 63

20.11.2MG18.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
ACTCAGTCTC	CAGACTCCCT	GGCIGTGTCT	CTGGGCGAGA	GGGCCACCAT	50
T Q S P	D S L	A V S	L G E R	A T I	
CAACTGCAAG	TCCAGCCAGA	GIGITTTTATA	CGGCTCCAAG	AATCAGAACT	100
N C K	S S Q S	V L Y	G S K	N Q N Y	
ACTTAGCTTG	GTACCAGCAG	AAACCAGGAC	AGCCTCCTAA	GCTGGTCATT	150
L A W	Y Q Q	K P G Q	P P K	L L I	
TACTGGGCAT	CTACCCGGGA	ATCCGGGGTC	CCTGACCGAT	TCAGGGGCAG	200
Y W A S	T R E	S G V	P D R F	R G S	
CGGGTCTAGG	ACAGATTICA	CTCTCACCAT	CAGCAGCCTG	CAGGCTGAAG	250
G S R	T D F T	L T I	S S L	Q A E D	
ATGTGGCAGT	TTACTTCTGT	CACCAATATT	ATAGTACTCC	GTTGCAOGTTC	300
V A V	Y F C	H Q Y Y	S T P	W T F	
GGCCAAGGGA	CCAAGGTGGA	AATCAAACGA	ACTGTGGCTG	CACCATCTGT	350
G Q G T	K V E	I K R	T V A A	P S V	
CTTCATCTTC	CCGCCATCTG	ATGAGCAGTT	GAAATCTGGA	ACTGCTCTCTG	400
F I F	P P S D	E Q L	K S G	T A S V	
TTGTGTGGCT	GCTGAATAAC	TTGTATCCCA	GAAAGCCAAG	GACACGAAAG	450
V C L	L N N	L Y P R	K P R	T R K	
GTCANACCA	CCC	(SEQ ID NO: 26)			463
V X P T		(SEQ ID NO: 62)			

FIG. 64

E20.18MG30.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
CGGATCCNC	CTGGNIGGTC	CCTGAGACTC	TCTGTGCAG	CGTCIGGATT	50
R D P P	G W S	L R L	S C A A	S G F	
CATCTTCANT	AACATATINCA	TGCACTGGGT	CCGOCAGGCT	CCAGGCAAGG	100
I F X	N Y X M	H W V	R Q A	P G K G	
GGCTGGAGTG	GGTGGCAATT	ATATGGTATG	ATGGAAGTAG	CAAATACTAT	150
L E W	V A I	I W Y D	G S S	K Y Y	
GCAGACTCCG	NGAAGGGCCG	ATTCACCATC	TCCAGAGACA	ATTCCAAGAA	200
A D S X	K G R	F T I	S R D N	S K N	
CACGCTGTAT	CTGCAAATGA	ACAGCCTGAG	AGCCGAGGAC	ACGGCTGATG	250
T L Y	L Q M N	S L R	A E D	T A D V	
TATTACTGIG	CGAGAGACGG	TTGGGCCCAG	GTGGCTTCTC	GCTTCTGACT	300
L L C	E R R	L G H G	G F S	L L T	
ACTGGNGCNC	AGGGCAACNC	TGNCINACCG	TNTTCTTCAN	CCCTNTACNC	350
T G A Q	G N X	X X P	X S S X	L Y X	
AAGGGCCNCC	ATTNGGTCTT	TCCCCCTGG	NNNNCTGCT	CNATGNNNCA	400
R A X	I X S F	P P G	X P A	X X X T	
CCCTNCGACA	NONACAN	(SEQ ID NO: 27)			417
L R X	X X	(SEQ ID NO: 63)			

FIG. 65

E20.18VK.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
TTGTGGCTG	TGTCCTGTG	CGAGAGGNC	ACCATCAACT	GCAAGTCCAG	50
F V A V	S L G	E R X	T I N C	K S S	
CCAGAGTATT	TTATACAGCT	CCAACAATCA	AAACTTCTTA	GCTTGGTACC	100
Q S I	L Y S S	N N Q	N F L	A W Y Q	
AGCAGAAACC	AGGACAGCCT	CCGAAGTTGC	TCATTCTACTG	GGCATCTATT	150
Q K P	G Q P	P K L L	I Y W	A S I	
CGGGAATCCG	GGGTCCCTGA	CCGATTCTAGT	GGCAGCGGGT	CTGGGACAGA	200
R E S G	V P D	R F S	G S G S	G T D	
TTTCACTCTC	ACCATCAGCA	GCTTGCAGGC	TGAAGATGIG	GCAGTTTATT	250
F T L	T I S S	L Q A	E D V	A V Y Y	
ACTGTCAGCA	GTATTATAGT	ATTCCGTGCA	CTTTTGGCCA	GGGACCAAG	300
C Q Q	Y Y S	I P C T	F G Q	G T K	
CTGGAGATCA	AACGAACIGT	GGCTGCACCA	TCGTCTCTTCA	TCTTCCCGCC	350
L E I K	R T V	A A P	S V F I	F P P	
ATCTGATGAG	CCAAGNTTGA	AAATCTGGAA	CTGCTCTCTGT	TGTGTGCGCCT	400
S D E	P X L K	I W N	C L C	C V P C	
GCTTGAATAA	CTTCTATCCC	AGAGANGGCC	AAAGTCCTGT	GGAAGGTGGA	450
L N N	F Y P	R X G Q	S P V	E G G	
TAC	(SEQ ID NO: 28)				453
Y	(SEQ ID NO: 64)				

FIG. 66

E20.19.2MG30.Seq Sequence

10	20	30	40	50
1234567890	1234567890	1234567890	1234567890	1234567890
CTCACCIGCA	CTGICICIGG	TGGCICCATC	AGTAGTTACT	NTTGGAGNIG
L T C T	V S G	G S I	S S Y X	W X W
GATCCGGCAG	CCCGVAGGCA	AGGACICGA	GIGCATGGG	TGTTTCTATT
I R Q	P X G K	G L E	W I G	C F Y Y
ACAGNGGAG	CACCAACTAC	AACCCCTCCC	TNAAGAGICA	TGICACCATTA
X G S	T N Y	N P S L	K S H	V T I
TCAGTAGACA	CGIICACAGAA	CCAGTCTTAC	NIGAGCIGA	GCINTIGIGAC
S V D T	S K N	Q F Y	X K L S	X V T
CGNIGCGGAC	ACGGNCGNCA	ATAACTGNGC	NAGACATAGG	GGAGNAGTGN
X A D	T X X N	N X A	R D R	G X V X
NNIIGGCNINC	TACINIGACT	ACTGAGGCCA	GNGAACCNIG	GNICACAGTA
W X X	T X T	T E A X	E P W	X T V
ATCCNTAAGN	CTNNCAANCA	AANGNCGCCC	AANGGANAC	NNNCTNCGNC
I X K X	X X X Q	X X P	X X X X	X X X

(SEQ ID NO: 29) 350
(SEQ ID NO: 65)

FIG. 67

E20.19.2VK.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
TCCTTGGTAG	CGNGTCTTGG	CGAGAGGCC	ACCATCAACT	GCAAGTCCAG	50
S L V A	X L G	E R P	T I N C	K S S	
CCAGAGIGTT	TTATACNGCT	CCAAGAATCA	GAACACTTA	GCTTGGTACC	100
Q S V	L Y X S	K N Q	N Y L	A W Y Q	
AGCAGAAACC	AGGACAGCCT	CCTAAGCTGC	TCATTTACTG	GGCATCTACC	150
Q K P	G Q P	P K L L	I Y W	A S T	
CGGGAATCCG	GGGTCCCTGA	CCGATTTCAGG	GGCAGCGGGT	CTAGGACAGA	200
R E S G	V P D	R F R	G S G S	R T D	
TTTCACCTCTC	ACCATCAGCA	GCCTGCAGGC	TGAAGATGIG	GCAGTTTACT	250
F T L	T I S S	L Q A	E D V	A V Y F	
TCTGTCACCA	ATATTATAGT	ACTCCGTGGA	CGTTCCGGCCA	AGGGACCAAG	300
C H Q	Y Y S	T P W T	F G Q	G T K	
GTGGAAATCA	AACGAACIGT	GGCTGCACCA	TCTGTCCTTCA	TCTTCCCGCC	350
V E I K	R T V	A A P	S V F I	F P P	
ATCTGATGAG	CACCTTGAAA	TTCTGGAACT	GCCTCTGNTG	NGTGCCCTGCT	400
S D E	H L E I	L E L	P L X	X A C	
GAACNAACTC	TATCCCCAGA	GANGGCCCAA	AAGTIVCAAG	NNGGNNAGGC	450
T N S	I P R	X G P K	V S X	X X G	
NNGATAACGC	CTNITCNCCN	NCNINC	(SEQ ID NO: 30)		476
X I T P	X X X	X	(SEQ ID NO: 66)		

FIG. 68

20.20.21MG30.Seq Sequenc

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
AAGCCTTTTC	AGACCNIGCC	CTTCACCTGC	ACIGTCTCTG	GIGGCTCCAT	50
K P F Q	T X P	F T C	T V S G	G S I	
CAGCAGTGGT	GGTTACTACT	GGAGCTGGAT	CCGCCAGCAC	CCAGGGAAGG	100
S S G	G Y Y W	S W I	R Q H	P G K G	
GCCTCGAGTG	GATTGGGTAC	ATCTATAACA	GIGGGAGCAC	CTACTACAAC	150
L E W	I G Y	I Y N S	G S T	Y Y N	
CCGTCCCTCC	AGAGTCGAGT	TACCATATCA	GTAGACACGT	CTAAGAACCA	200
P S L Q	S R V	T I S	V D T S	K N Q	
GTCTCCCTG	AAGCTGAGCT	CTGTGACTGC	CCGGGACACG	GCCGTGTATT	250
F S L	K L S S	V T A	A D T	A V Y Y	
ACTGTGCGGG	TCAGAAATGG	TCCTACTACT	ACTACTACGG	TATGGACGTC	300
C A G	Q K W	S Y Y Y	Y Y G	M D V	
TGGGGCCAAG	GGACCAAGGT	CACCGTCTCC	TNAGCCTCCA	CCAANGGCCC	350
W G Q G	T T V	T V S	X A S T	X G P	
ATCGGTCTTC	CCCTGGGCGC	CCTGNTCTAG	GAGCACTCC	CANAGCACAG	400
S V F	P L A P	X S R	S T S	X S T D	
ACGGATNCTG	GGCCTGCCTG	NATCAATGGA	CTACTTTCCC	CGAACCGGTT	450
G X W	A C L	X Q W T	T F P	E P V	
GNNIGTGNNN	CCTGGNAACT	N	(SEQ ID NO: 31)		471
X C X X	W X L		(SEQ ID NO: 67)		

FIG. 69

E-20.22MG30.Seq Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
AAGCCTTNG	AGACCNIGCC	CCTCACTGC	ACTGTCTCTG	GTGGCTOCAT	50
K P X E	T X P	L T C	T V S G	G S I	
CAGTAATTAC	TACTGGAGCT	GGATCGGCA	GCCCCAGGG	AAGGGACTGG	100
S N Y	Y W S W	I R Q	P P G	K G L E	
AGTGGATTGG	GTATATCTAT	TACAGTGGGA	GCAOCAAATA	CAACCCCTCC	150
W I G	Y I Y	Y S G S	T N Y	N P S	
CTCAAGAGTC	GAGTCACCAT	ATCAGTAGAC	ACGTCCAAGA	ACCAGTCTTC	200
L K S R	V T I	S V D	T S K N	Q F S	
CCTGAAGCTG	AGCTCTGIGA	CCGCTGCGGA	CACGGGCGTG	TATTACTGIG	250
L K L	S S V T	A A D	T A V	Y Y C A	
CGAGAGGGCC	CGGGGGGAGC	TACTACTACT	ACGGTATGGA	CGTCTGGGGC	300
R G P	G G S	Y Y Y Y	G M D	V W G	
CAAGGGACCA	CGGTACCGT	CTCCTCAGCC	TCCACCAAGG	GOCCATCGGT	350
Q G T T	V T V	S S A	S T K G	P S V	
CTTCCCCCTG	GCGCCCTGCT	CCAGGAGCAC	CTCCGAGAGC	ACAGCGGGCC	400
F P L	A P C S	R S T	S E S	T A A L	
TGGGCTGGCT	GGGTCAAGGA	CTACTTCCCC	GAACGGGIGA	CGGTGTTCGN	450
G C L	G Q G	L L P R	T G D	G V R	
NGGAC	(SEQ ID NO: 32)				456
X N	(SEQ ID NO: 68)				

FIG. 70

Amino Acid Sequences and Structure of Human Heavy Chain Derived from EGFR-Specific Hybridomas

Human $\gamma 2$	CDR1	CDR2	CDR3	ASTKGPSVFPPLAPCSRSTST	(SEQ ID NO: 73)
4-31	VSGGSISSGGTYNEMIRQHPGKGLNIGIYVTSGETTNPISLKSRTVLSVDTSNQPSLKLSVTAAADTAVTYCAR				(SEQ ID NO: 35)
1.1	---D---DC---	---	STVNPG WDP	WQGGTLVTVSS	(SEQ ID NO: 31)
E2.4	---D---S---H-P---	---	NIVTGG AFDI	WQGGTNVTVSS	(SEQ ID NO: 41)
E2.5	---D---S---H---	---	KPVVGG EDY	WQGGTLVTVSS	(SEQ ID NO: 43)
E6.2	---D---DP---	---	ESLYTGG GMDV	WQGGTVTVTVSS	(SEQ ID NO: 45)
E6.4	---D---H-D---	---	GVVTVV YFDY	WQGGTVTVTVSS	(SEQ ID NO: 47)
E20.21	---C---	---	QKNSYYYYYGMV	WQGGTVTVTVSS	(SEQ ID NO: 75)
Human $\gamma 1$	CDR1	CDR2	CDR3		
4-61	VSGGSISSGGTYNEMIRQHPGKGLNIGIYVTSGETTNPISLKSRTVLSVDTSNQPSLKLSVTAAADTAVTYCAR				(SEQ ID NO: 38)
E2.11	---D---DC---	---	DPLTGGP FDY	WQGGTNVTVSS	(SEQ ID NO: 49)
E6.3	---D---S---H---	---	DSILGA TNY	WQGGTLVTVSS	(SEQ ID NO: 51)
E7.6.3	---D---S---H---	---	V-DRTCA FDI	WQGGTNVTVSS	(SEQ ID NO: 53)

FIG. 71

E7.5.2.K.aa Sequence

10	20	30	40	50
1234567890	1234567890	1234567890	1234567890	1234567890
CTGTCIGCAT	CTGTAGGACA	CAGAGTCATA	ATCACTIGCC	GGCAAGTCA
50				
L S A S	V G D R	V I I T	C R A S	Q
AAACATCACC	GACCATTTAA	ATTGGTATCA	GCAGATAGCA	GGAAAAGCCC
100				
N I T D	H L N W	Y Q Q I	A G K A	P
CTAGGCCOCT	GATATACACT	GCATCCAGTT	TGCAAGGIGG	GGTCCCATCA
150				
R P L I	Y T A S	S L Q G	G V P S	
AGGTCAGIG	GCAGIGGATC	TGGACAGAT	TTCATCTCA	CCATCAGCAG
200				
R F S G	S G S G	T D F T	L T I S	S
TCGTCAACCT	GAACATTTTT	CAACTTACTA	CTGCAACAG	AGTTACAGTA
250				
L Q P E	D F S T	Y Y C Q	Q S Y S	T
CCCCGIGCAG	TTTIGGCCAG	GGGACCAAGC	TGGAGATCAA	ACGAACGIG
300				
P C S F	G Q G T	K L E I	K R T V	
GCTGCACCAT	CTGTCTTCAT	CTTCCCGCCA	TCGTATGAGC	AGTTGAATC
350				
A A P S	V F I F	P P S D	E Q L K	S
TGGAACIGCC	TCGTGTGIGT	GCCTCGCGAA	TAACTTCTAT	CCCA
394				
G T A S	V V C L	L N N F	Y P	

FIG. 72

E7.5.2.v.aa Sequence

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
GTGAAGGICT	CCTGCAAGGC	TTCTGGATAC	ACCTTCAGCG	GCTACTATAT	50
V K V S	C K A	S G Y	T F S G	Y Y M	
GCCTGGGTG	CGACAGGCC	CTGGACAAGG	GCTTGAGTGG	ATGGGATCGA	100
H W V	R Q A P	G Q G	L E W	M G S I	
TCCACCTAA	CAGTGGTGGC	ANAACTTTG	CACAGAAGTT	TCAGGGCAGG	150
H P N	S G G	X N F A	Q K F	Q G R	
GTCACCATGA	CCAGGGACAC	GTCCATCAAC	ACAGCCTACT	TGGAGCTGAG	200
V T M T	R D T	S I N	T A Y L	E L S	
CAGGCTGAGA	TCTGACGACA	CGGCCGTGTA	TTACTGTGCG	AGAGATAAAA	250
R L R	S D D T	A V Y	Y C A	R D K N	
ACTACGGTGA	CTACGTCCTT	GACTATTGGG	GCCAGGGAAC	CCTGGTCACC	300
Y G D	Y V F	D Y W G	Q G T	L V T	
GTCTCTCAG	(SEQ ID NO: 34)				310
V S S	(SEQ ID NO: 70)				

FIG. 73

Effect of E7.6.3 or E7.5.2 on human epidermoid carcinoma A431 growth in nude mice

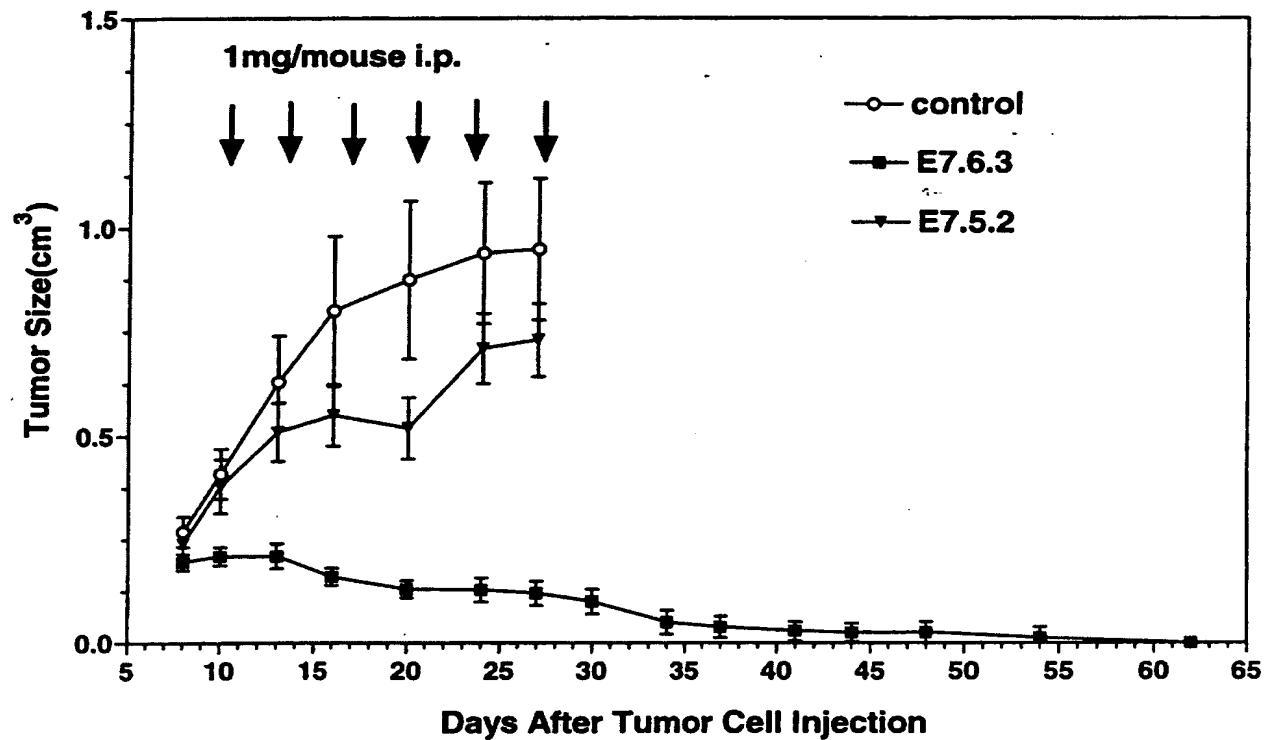


FIG. 74

**Effect of E7.6.3 on human pancreatic carcinoma HPAC
growth in nude mice**

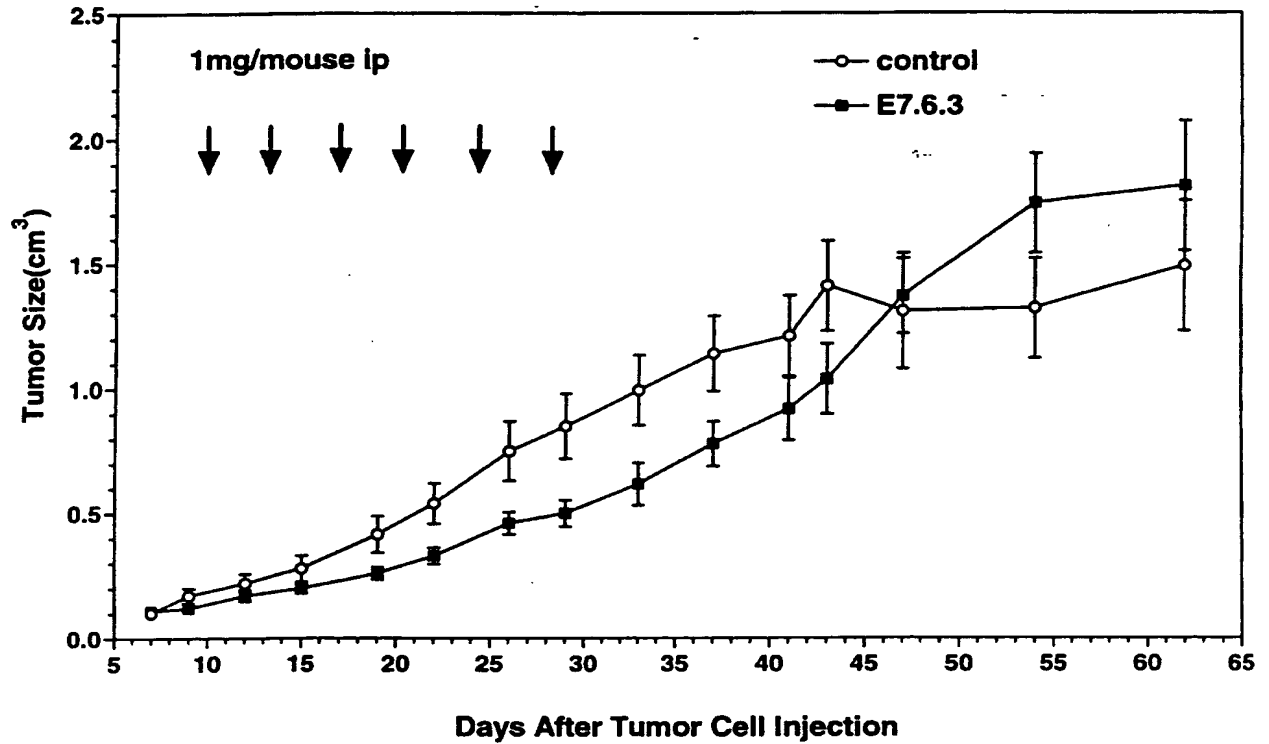


FIG. 75

Effect of E7.6.3 on human pancreatic carcinoma BxPC-3 growth in nude mice

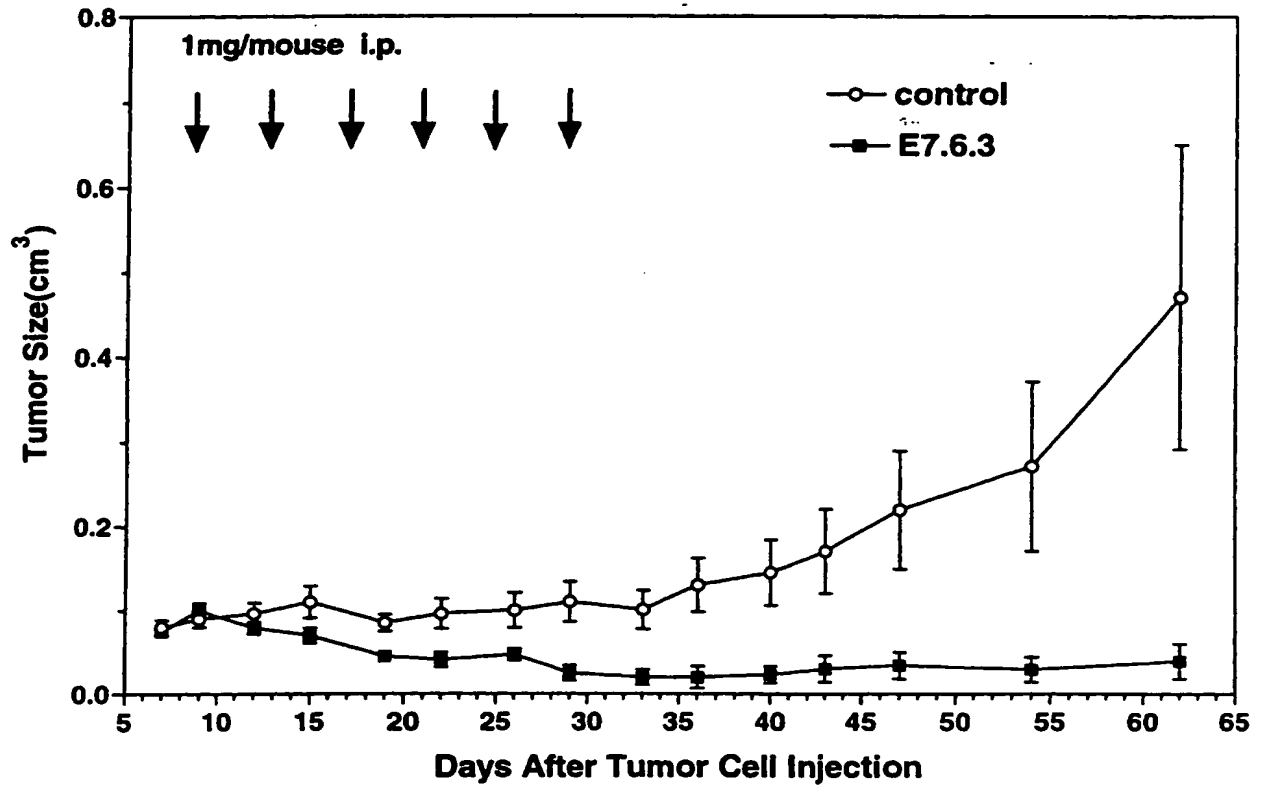


FIG. 76

Effect of E7.6.3 on HS766T Pancreatic tumor growth in nude mice

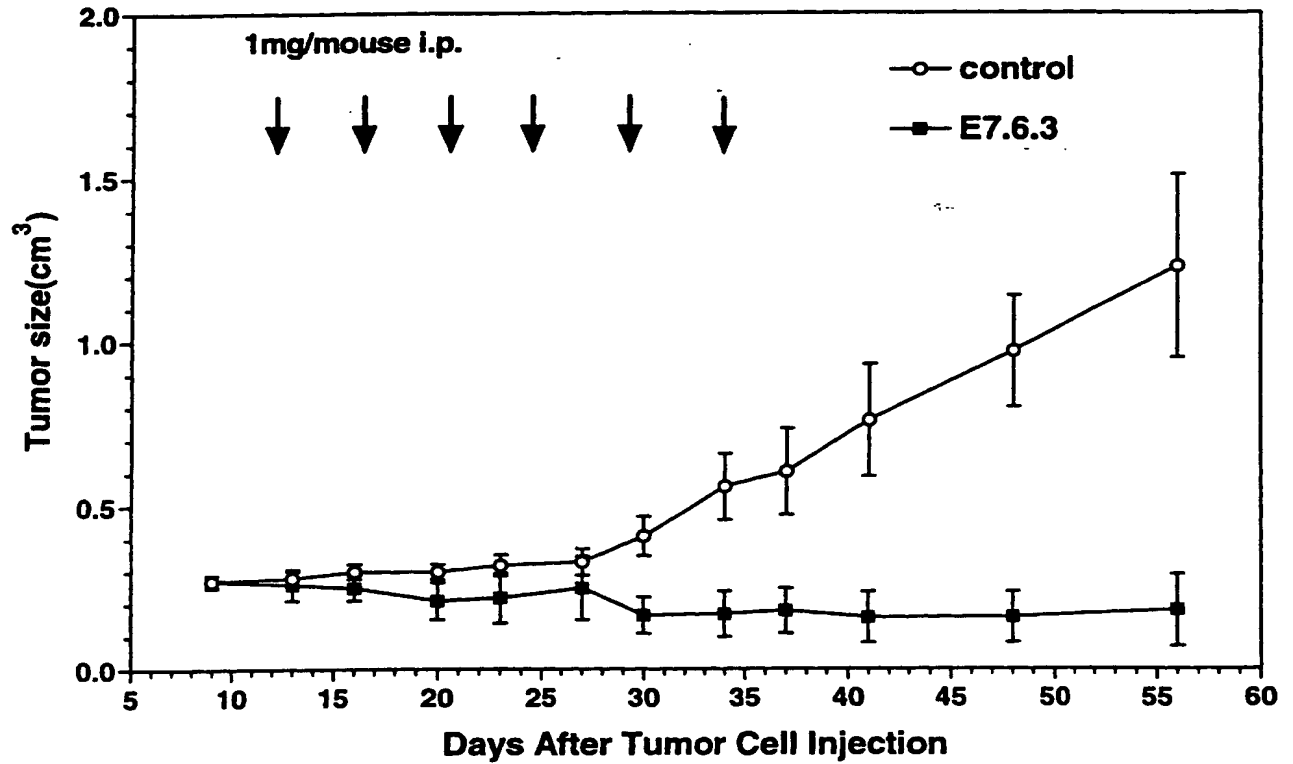


FIG. 77

**Effect of E7.6.3 on SK-RC-29 human kidney
carcinoma growth in nude mice**

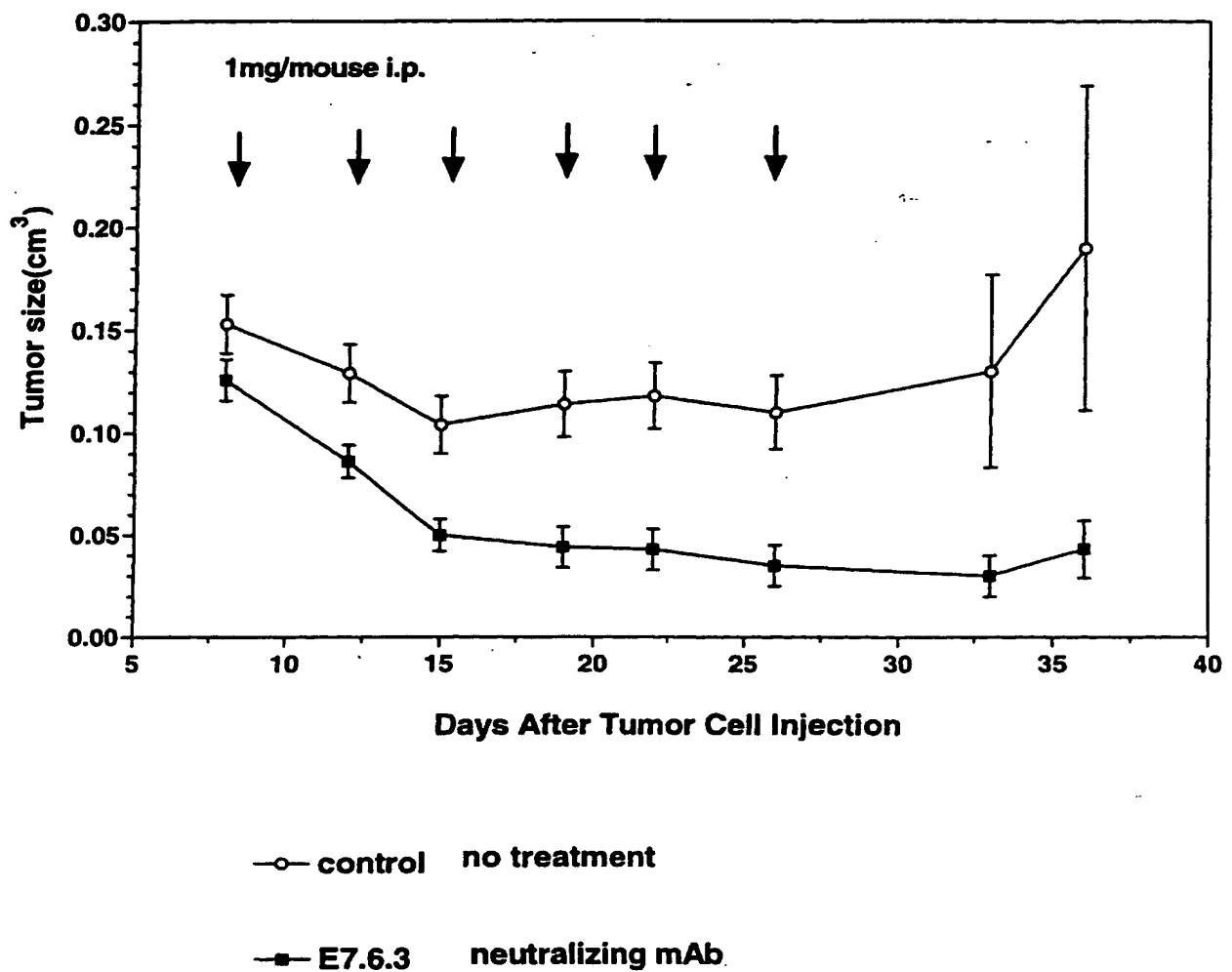


FIG. 78

**Effect of E7.6.3 on human colon carcinoma
SW707 (EGFr-) growth in nude mice**

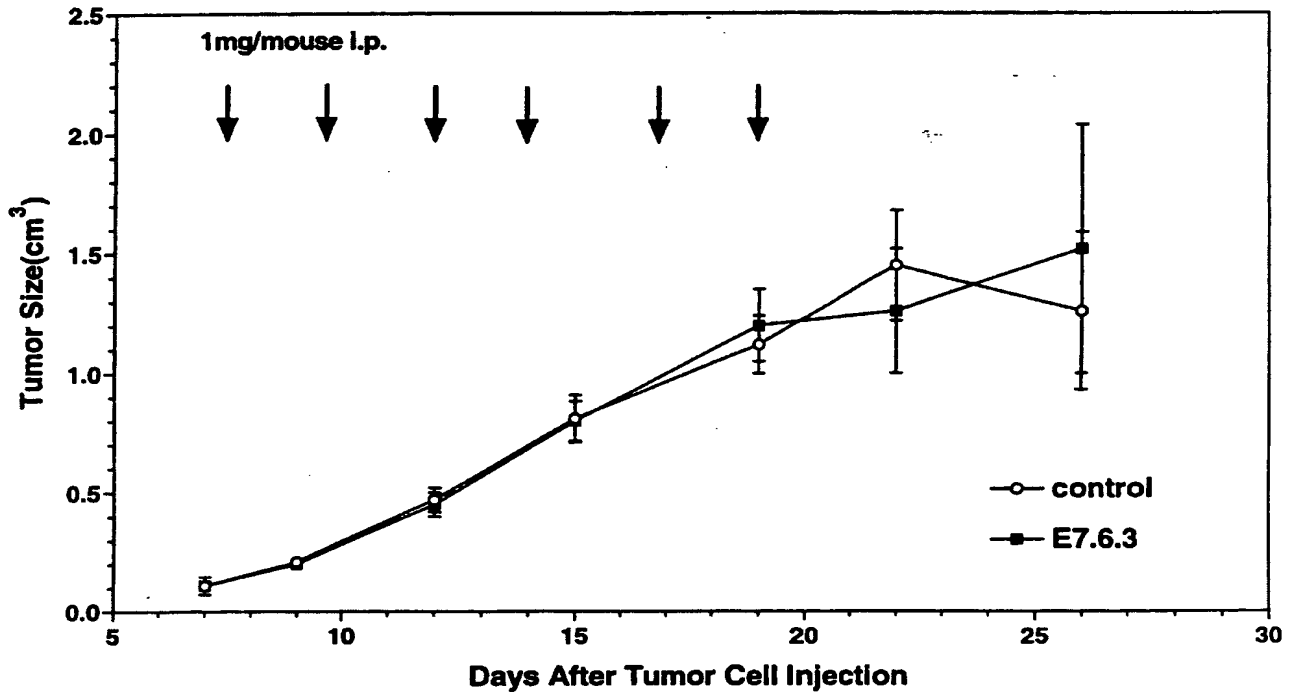
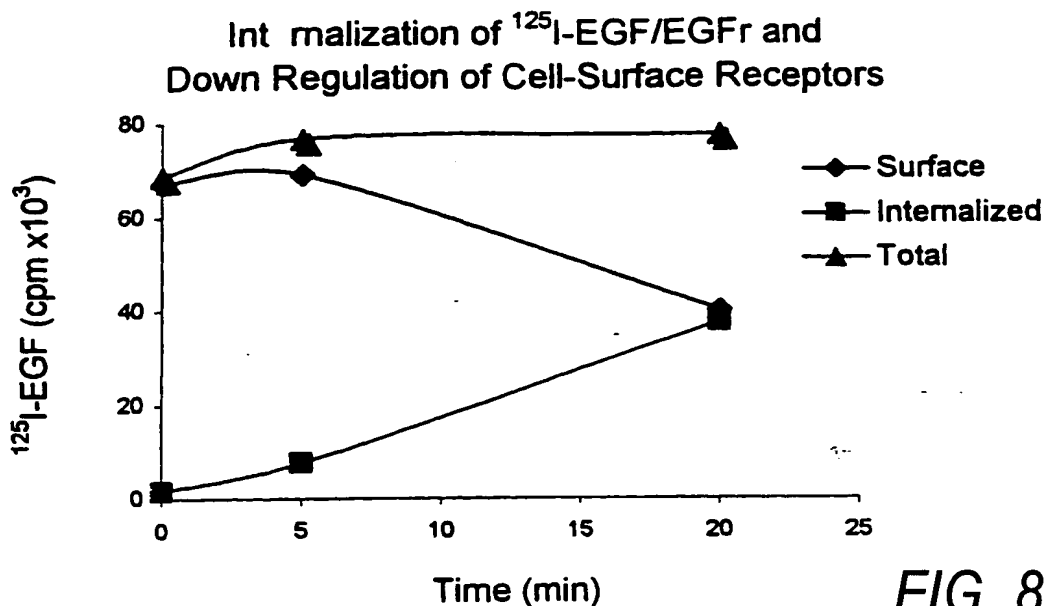
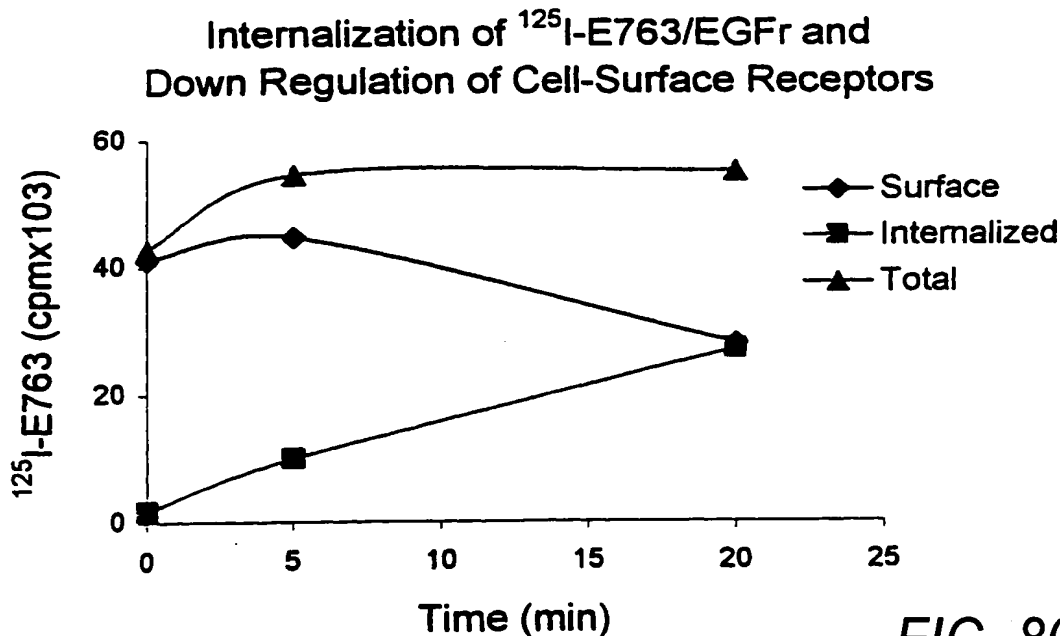


FIG. 79



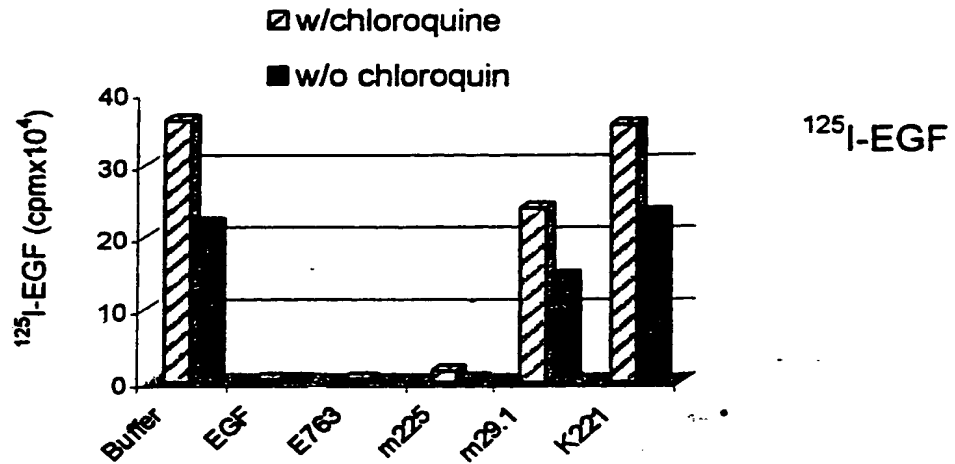
^{125}I -EGF	Time (min)	Surface	Internalize	Total	% internalized
	0	67.153	1.515	68.668	2.2
	5	68.997	7.649	76.646	10
	20	39.986	37.406	77.392	48



^{125}I -E763	Time (min)	Surface	Internalize	Total	% internalized
	0	41.051	1.684	42.735	3.9
	5	44.567	9.876	54.443	18
	20	27.969	26.998	54.967	49

Degradation of ^{125}I -EGF or ^{125}I -E76.

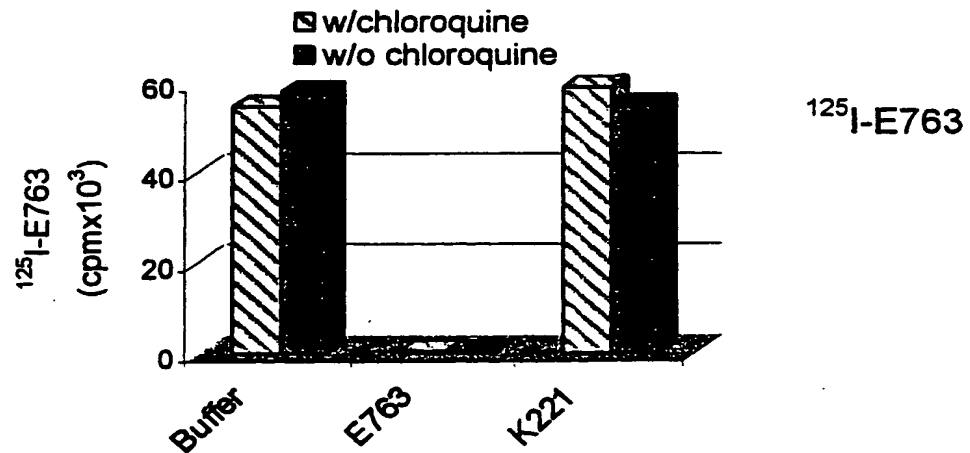
A431 c



w/ or w/o chloroquine (100 μM)

		w/chloroq	w/o chloroquine	% degradation	% competition
cpm $\times 10^4$	Buffer	36.0898	21.8277	40	0
	EGF	0.3684	0.3776		98
	E763	0.481	0.2132		99
	m225	1.5468	0.4882		98
	m29.1	23.9704	14.459		34
	K221	35.5084	23.2694	34	1.6

FIG. 81A



w/ or w/o chloroquine (100 μM)

		w/chloroq	w/o chloroquine	% degradation	% competition
cpm $\times 10^4$	Buffer	54.608	57.824	0	0
	E763	0.536	0.441		99
	K221	58.956	54.83	7	5

FIG. 81B

Effects of E763 and m225 on EGFr degradation

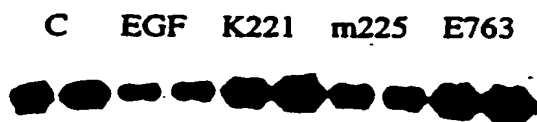


FIG. 82A

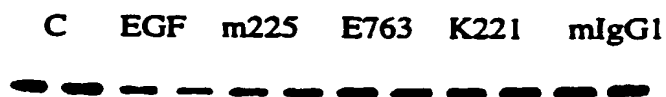


FIG. 82B

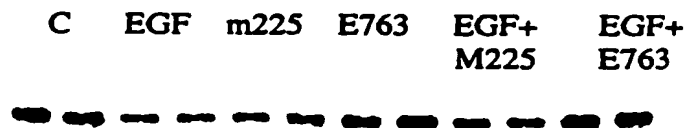


FIG. 82C

Effect of E763 and m225 on EGFr threonine phosphorylation

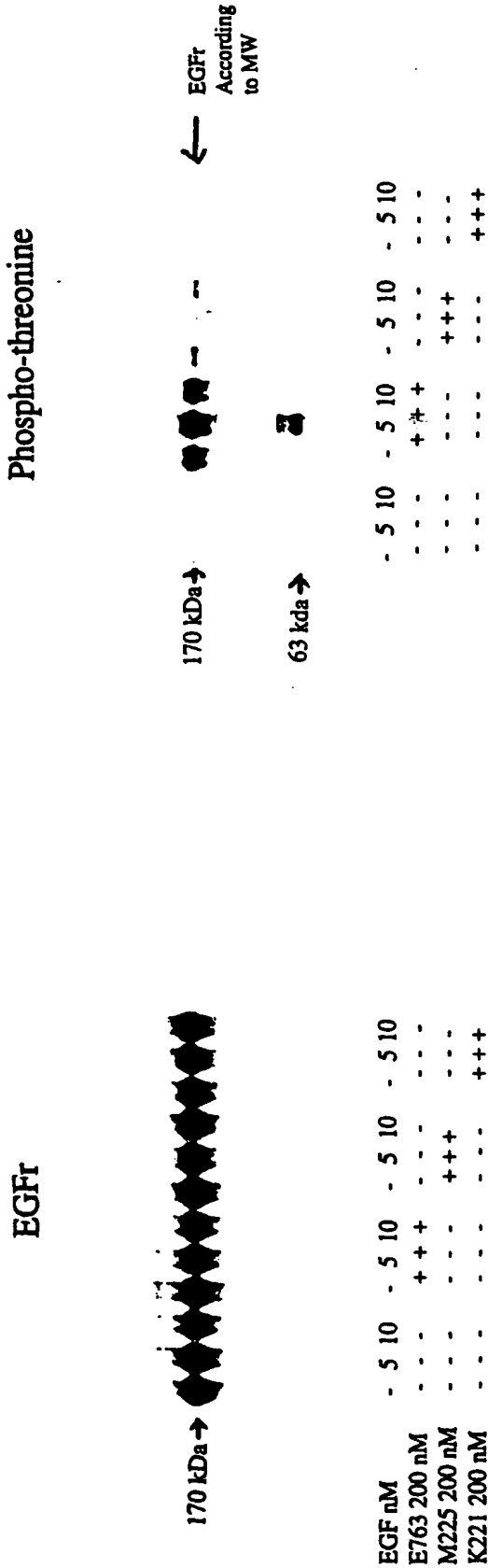


FIG. 83A

FIG. 83B

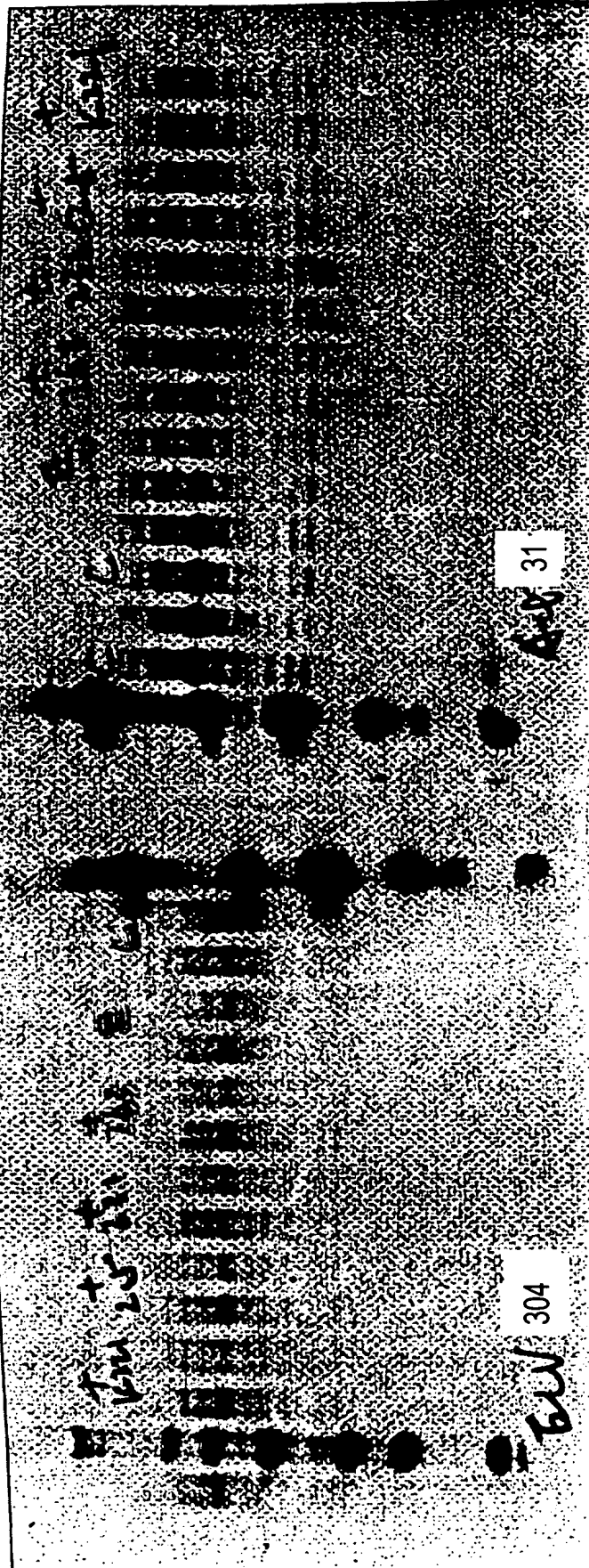


FIG. 84

E763 on VEGF secretion

Effects of E763 and m225 on VEGF secretion in cultured A431 cells

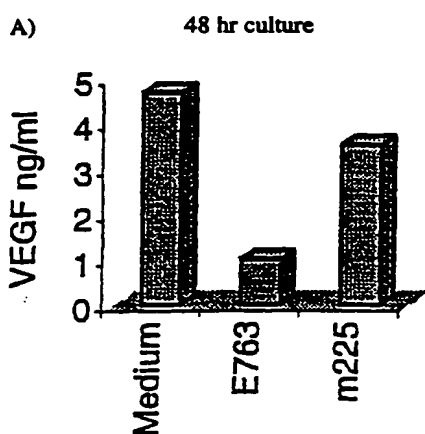


FIG. 85A

Effects of E763 and E752 on VEGF secretion in cultured A431 cells

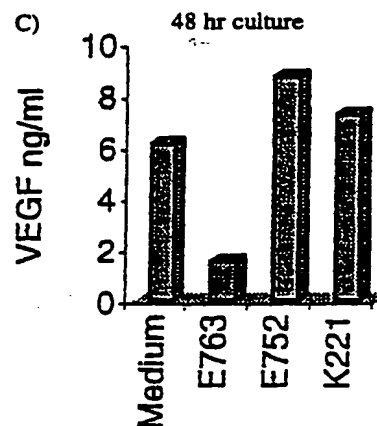


FIG. 85B

Effects of E763 and E752 on VEGF secretion in cultured A431 cells (24 hr)

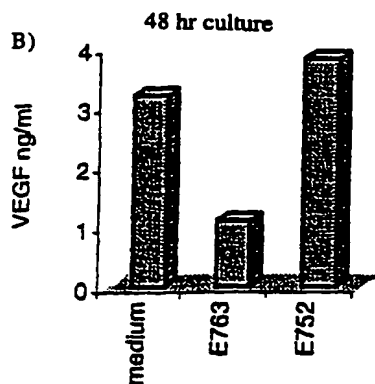


FIG. 85C

Effect of E763 on VEGF secretion in cultured A431 cells

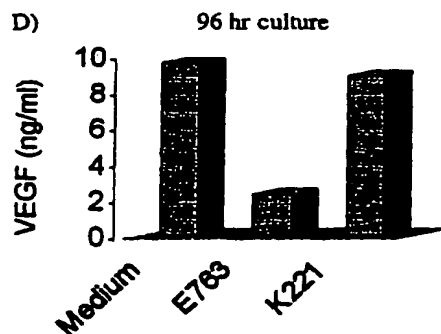
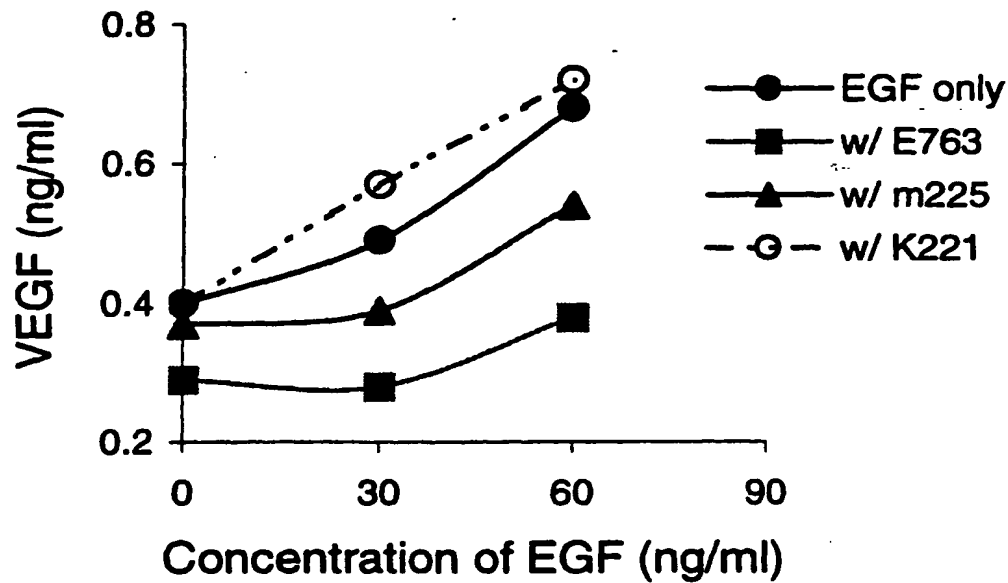


FIG. 85D

Effects of E763 and m225 on VEGF secretion in cultured endothelial cells



11/5/98 VEGF in endothelial cells (ECV304)(ATTCC, CRL-1998)
 VEGF ng/ml no serum

	0	30	60
EGF only	0.4	0.49	0.68
w/ E763	0.29	0.28	0.38
w/ m225	0.37	0.39	0.54
w/ K221	0.4	0.57	0.72

FIG. 86